Search Strategy

FILE 'USPATFULL' ENTERED AT 15:58:11 ON 16 OCT 2000

		E	KITTO GEORGE BARRIE/IN
L1	2	S	E3
		E	KITTO GEORGE B/IN
L2	1	S	E2
		E	BURNETT MARY SUSAN/IN
L3	158	S	VACCINE (5W) VECTOR
L4	44	S	L3 AND SALMONELLA
L5	11	S	L4 AND SALMONELLA/CLM
L6	33	S	L4 NOT L5
L7	20	S	L6 AND (EXPRESSION VECTOR)
L8	18	S	L7 AND (ATTENUAT? OR AVIRULENT)
L9	56	S	(SALMONELLA (2W) ATTENUAT?) OR (SALMONELLA (2W) AVIRULENT)
L10	7	S	L9 AND ATTENUAT?/CLM
L11	7	S	L10 NOT L8

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		E	KITTO G B/IN
L12	3	S	E3
		E	BURNETT M S/IN
L13	2	S	E3
L14	1	S	L13 NOT L12
L15	129	S	(VACCINE (5W) VECTOR)
L16	9	S	L15 AND SALMONELLA
L17	9	S	L16 NOT L12
L18	4790	S	EXPRESSION VECTOR
L19	34	S	L18 AND SALMONELLA
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L21	7	S	L20 NOT L17

FILE 'MEDLINE' ENTERED AT 16:37:31 ON 16 OCT 2000

		E	KITTO G B/AU
L22	42	S	E3
L23	0	S	L22 AND SALMONELLA
L24	1	S	L22 AND VACCIN?
L25	0	S	L22 AND (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)
		E	BURNETT M S/AU
L26	1	S	E3
L27	45614	S	SALMONELLA
L28	2217	S	L27 AND VACCIN?
L29	646	S	L28 AND (ATTENUAT? OR AVIRULENT)
L30	136	S	L29 AND (RECOMBINANT PROTEIN OR HETEROLOGOUS OR FOREIGN)
L31	35	S	L30 AND VECTOR

FILE 'USPATFULL' ENTERED AT 16:48:32 ON 16 OCT 2000

L32	32391	S	COLI
L33	1405	S	L32 AND LIPOPROTEIN
L34	415	S	L33 AND (SIGNAL SEQUENCE)
L35	257	S	L34 AND (FUSION PROTEIN?)
L36	62	S	L35 AND (OUTER MEMBRANE PROTEIN OR OMPA)
L37	14	S	L36 AND SIGNAL/CLM

FILE 'MEDLINE' ENTERED AT 16:57:14 ON 16 OCT 2000

L38	191707	S	COLI
L39	876	S	L33 AND LIPOPROTEIN
L40	84	S	L39 AND (SIGNAL SEQUENCE)
L41	18	S	L40 AND (OMP? OR OUTER MEMBRANE PROTEIN)
L42	6833	S	EXPRESSION VECTOR
L43	9317	S	SIGNAL SEQUENCE OR SIGNAL PEPTIDE
L44	26	S	LIPOPROTEIN SIGNAL SEQUENCE

L5 ANSWER 2 OF 11 USPATFULL
2000:80857 Genetically modified tumor-targeted bacteria with reduced virulence.
Bermudes, David, Wallingford, CT, United States
Low, Kenneth Brooks, Guilford, CT, United States
Vion Pharmaceuticals, Inc., New Haven, CT, United States (U.S. corporation)Yale University, New Haven, CT, United States (U.S. corporation)
US 6080849 20000627
APPLICATION: US 1997-926636 19970910 (8)
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed to mutant ***Salmonella*** sp. having a genetically modified msbB gene in which the mutant ***Salmonella*** is capable of targeting solid tumors. The present invention further relates to the therapeutic use of the mutant ***Salmonella*** for growth inhibition and/or reduction in volume of solid tumors.

CLM What is claimed is:

1. A mutant ***Salmonella*** sp. comprising a genetically modified msbB gene in a tumor targeting mutant ***Salmonella*** which is capable of inhibiting growth of a solid tumor when administered in vivo, wherein said mutant ***Salmonella*** sp. expresses an altered lipid A molecule compared to a wild-type ***Salmonella*** sp., and induces TNF.alpha. expression at a level less than that induced by a wild type ***Salmonella*** sp.

2. The mutant ***Salmonella*** of claim 1 which is designated YS1629 and having ATCC Accession No. 202025 or is designated YS1170 and having ATCC Accession No. 202024 or is designated YS8211 and having ATCC Accession No. 202026.

3. The mutant ***Salmonella*** of claim 1 which is selected from the group consisting of ***Salmonella*** typhi, ***Salmonella*** choleraesuis, and ***Salmonella*** enteritidis.

4. The mutant ***Salmonella*** of claim 1 which induces TNF.alpha. expression at about 5 percent to about 40 percent of that induced by a wild type ***Salmonella*** sp.

5. The mutant ***Salmonella*** of claim 1 which induces TNF.alpha. expression at about 10 percent to about 35 percent of that induced by a wild type ***Salmonella*** sp.

6. The mutant ***Salmonella*** of claim 1 in which a chelating agent inhibits growth of mutant ***Salmonella*** by about 90 percent compared to the growth of a wild type ***Salmonella*** sp.

7. The mutant ***Salmonella*** of claim 1 in which a chelating agent inhibits growth of mutant ***Salmonella*** by about 99 percent compared to the growth of a wild type ***Salmonella*** sp.

8. The mutant ***Salmonella*** of claim 1 in which a chelating agent inhibits growth of mutant ***Salmonella*** greater than 99 percent compared to the growth of a wild type ***Salmonella*** sp.

9. The mutant ***Salmonella*** of claim 6, 7, or 8 in which the chelating agent is selected from the group consisting of Ethylenediaminetetraacetic Acid (EDTA), Ethylene Glycol-bis(P-aminoethyl Ether) N,N,N',N',-Tetraacetic Acid (EGTA) and sodium citrate.

10. The mutant ***Salmonella*** of claim 1 which survives in macrophages at about 50 percent to about 30 percent of the level of survival of a wild type ***Salmonella*** sp.

11. The mutant ***Salmonella*** of claim 1 which survives in macrophages at about 30 percent to about 10 percent of the level of survival of a wild type ***Salmonella*** sp.

12. The mutant ***Salmonella*** of claim 1 which survives in macrophages at about 10 percent to about 1 percent of the level of survival of a wild type ***Salmonella*** sp.

13. A pharmaceutical composition comprising an amount of the mutant ***Salmonella*** of claim 1 effective to inhibit growth or reduce volume of a solid tumor; and a pharmaceutically acceptable carrier.

L5 ANSWER 5 OF 11 USPATFULL
1999:27618 Method for introducing and expressing genes in animal cells and live invasive bacterial vectors for use in the same.
Powell, Robert J., Baltimore, MD, United States
Lewis, George K., Baltimore, MD, United States
Hone, David M., Ellicott City, MD, United States
University of Maryland at Baltimore, Baltimore, MD, United States (U.S. corporation)
US 5877159 19990302
APPLICATION: US 1995-433790 19950503 (8)
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method for introducing and expressing genes in animal cells is disclosed comprising infecting said animal cells with live invasive bacteria, wherein said bacteria contain a eukaryotic expression cassette encoding said gene. The gene may encode, e.g., a vaccine antigen, an therapeutic agent, an immunoregulatory agent or a anti-sense RNA or a catalytic RNA.
CLM What is claimed is:
1. A method for introducing and expressing a gene in animal cells comprising infecting said animal cells with live invasive bacteria, wherein said bacteria contain a eukaryotic expression cassette encoding said gene, wherein said gene encodes a vaccine antigen, wherein said vaccine antigen is expressed at detectable levels, and wherein said animals cells are cultured in vitro.

2. The method of claim 1, wherein said animal cell is a mammalin cell.

3. The method of claim 2, wherein said mammalian cell is selected from the group consisting of human, bovine, ovine, porcine, feline, buffalo, canine, goat, equine, donkey, deer, and primate cells.

4. The method of claim 3, wherein said mammalian cell is human cells.

5. The method of claim 1, wherein said invasive bacteria is selected from the group consisting of Shigella spp, Listeria spp., Rickettsia spp and enteroinvasive Escherichia coli.

6. The method of claim 5, wherein said invasive bacteria is attenuated.

7. The method of claim 1, wherein said invasive bacteria is selected

from the group consisting of Yersinia spp., Escherichia spp., Klebsiella spp., Bordetella spp., Neisseria spp., Aeromonas spp., Franciesella spp., Corynebacterium spp., Citrobacter spp., Chlamydia spp., Hemophilus spp., Brucella spp., Mycobacterium spp., Legionella spp., Rhodococcus spp., Pseudomonas spp., Helicobacter spp., ***Salmonella*** spp., Vibrio spp., Bacillus spp., Leishmania spp. and Erysipelothrix spp. which have been genetically engineered to mimic the invasion properties of Shigella spp., Listeria spp., Rickettsia spp., or enteroinvasive E. coli spp.

8. The method of claim 7, wherein said invasive bacteria is attenuated.

9. The method of claim 1, wherein said animal cells are infected with about 10.sup.3 to 10.sup.11 viable invasive bacteria.

10. The method of claim 9, wherein said animal cells are infected with about 10.sup.5 to 10.sup.9 viable invasive bacteria.

11. The method of claim 1, wherein said animal cells are infected at a multiplicity of infection ranging from about 0.1 to 10.sup.6.

12. The method of claim 11, wherein said animal cells are infected at a multiplicity of infection ranging from about 10.sup.2 to 10.sup.4.

13. A method for introducing and expressing a gene in animal cells comprising infecting said animal cells with live invasive Shigella spp., wherein said Shigella spp. contain a eukaryotic expression cassette encoding said gene, wherein said gene encodes a vaccine antigen, wherein said vaccine antigen is expressed at detectable levels, and wherein said animals cells are cultured in vitro.

14. The method of claim 1, wherein said Shigella spp is Shigella flexneri.

15. A method for inducing an immune response in an animal comprising infecting said animal with attenuated live invasive bacteria, wherein said bacteria contain a eukaryotic expression cassette encoding said gene, wherein said gene encodes a vaccine antigen, wherein said vaccine antigen is expressed at levels sufficient to induce an immune response, wherein said invasive bacteria are administered to a mucosal surface of said animal.

16. The method of claim 13, wherein said invasive bacteria are intranasally administered to said animal.

17. The method of claim 15, wherein said animal is a human.

18. The method of claim 15, wherein said attenuated bacteria is attenuated Shigella spp. or attenuated ***Salmonella*** spp.

19. The method of claim 16, wherein said animal is a mammal.

20. The method of claim 17, wherein said invasive bacteria are intranasally administered to said human.

21. The method of claim 19, wherein said invasive bacteria are intranasally administered to said mammal.

22. The method of claim 18, wherein said attenuated bacteria is

attenuated Shigella spp. is Shigella flexneri.

23. The method of claim 15, wherein said invasive bacteria is selected from the group consisting of Shigella spp, Listeria spp., Rickettsia spp and enteroinvasive Escherichia coli.

24. The method of claim 15, wherein said invasive bacteria is selected from the group consisting of Yersinia spp., Escherichia spp., Klebsiella spp., Bordetella spp., Neisseria spp., Aeromonas spp., Franciesella spp., Corynebacterium spp., Citrobacter spp., Chlamydia spp., Hemophilus spp., Brucella spp., Mycobacterium spp., Legionella spp., Rhodococcus spp., Pseudomonas spp., Helicobacter spp., ***Salmonella*** spp., Vibrio spp., Bacillus spp., Leishmania spp. and Erysipelothrix spp. which have been genetically engineered to mimic the invasion properties of Shigella spp., Listeria spp., Rickettsia spp., or enteroinvasive E. coli spp.

L5 ANSWER 9 OF 11 USPATFULL
97:70928 Recombinant avirulent ***salmonella*** antifertility vaccines.
Curtiss, III, Roy, St. Louis, MO, United States
Tung, Kenneth S. K., Charlottsville, VA, United States
Washington University, St. Louis, MO, United States (U.S. corporation)
US 5656488 19970812
APPLICATION: US 1994-222182 19940401 (8)
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

102/103

AB Avirulent microbes which include a recombinant expression system encoding a gamete-specific antigen, are disclosed. The microbes can be used in compositions to immunize a vertebrate subject against the gamete-specific antigen, thereby preventing or reducing conception rates in the subject to which they are administered.

CLM What is claimed is:

1. An avirulent microbe derived from a pathogenic gram negative microorganism selected from the group consisting of ***Salmonella*** , Escherichia, and ***Salmonella*** -Escherichia hybrids comprising a recombinant expression system which encodes at least one gamete-specific antigen that is displayed on the surface of gametes exposed during the process leading to fertilization, wherein the avirulent microbe, upon administration to an individual, is capable of colonizing a lymphoreticular tissue and eliciting a mucosal immune response.

2. An avirulent microbe according to claim 1, wherein the avirulent microbe lacks a functioning native chromosomal gene encoding beta-aspartate semialdehyde dehydrogenase (Asd), and further wherein the microbe comprises a recombinant gene encoding a functional Asd polypeptide, the recombinant gene being linked to one or more genes encoding one or more gamete-specific antigens.

3. An avirulent microbe according to claim 1, wherein the avirulent microbe comprises a mutated cya gene such that the microbe is substantially incapable of producing functional adenylate cyclase.

4. An avirulent microbe according to claim 1, wherein the avirulent microbe comprises a mutated crp gene such that the microbe is substantially incapable of producing functional cyclic AMP receptor protein.

5. An avirulent microbe according to claim 2, wherein the avirulent

microbe further comprises a mutated cya gene and a mutated crp gene such that the microbe is substantially incapable of producing functional adenylate cyclase and functional cyclic AMP receptor protein.

6. An avirulent microbe according to claim 1, wherein the microbe is S. typhimurium.

7. An avirulent microbe according to claim 1, wherein the microbe is an E. coli- ***Salmonella*** hybrid.

8. An avirulent microbe according to claim 1, wherein the gamete-specific antigen is lactic dehydrogenase-C.

9. An avirulent microbe according to claim 1, wherein the gamete-specific antigen is SP-10.

10. An avirulent microbe according to claim 1 wherein the gamete-specific antigen is ZP-3.

11. An avirulent microbe according to claim 5, wherein the gamete-specific antigen is lactic dehydrogenase-C.

12. An avirulent microbe according to claim 5, wherein the gamete-specific antigen is SP-10.

13. An avirulent microbe according to claim 5 wherein the gamete-specific antigen is ZP-3.

14. A vaccine composition comprising a therapeutically effective amount of an avirulent microbe according to claim 1, in combination with a pharmaceutically acceptable vehicle.

15. A vaccine composition comprising a therapeutically effective amount of an avirulent microbe according to claim 5, in combination with a pharmaceutically acceptable vehicle.

16. A method for inducing an antifertility state in a vertebrate subject, said method comprising administering to said subject an effective amount of a vaccine composition according to claim 14.

17. A method for inducing an antifertility state in a vertebrate subject, said method comprising administering to said subject, an effective amount of a vaccine composition according to claim 15.

18. A method according to claim 16, wherein the gamete-specific antigen is lactic dehydrogenase-C.

19. A method according to claim 16, wherein the gamete-specific antigen is SP-10.

20. A method according to claim 16, wherein the gamete-specific antigen is ZP-3.

21. A method according to claim 17, wherein the gamete-specific antigen is lactic dehydrogenase-C.

22. A method according to claim 17, wherein the gamete-specific antigen is SP-10.

23. A method according to claim 17, wherein the gamete-specific antigen is ZP-3.

24. An avirulent microbe according to claim 1 wherein the gamete-specific antigen is a sperm-specific antigen.

25. An avirulent microbe according to claim 24 wherein the sperm-specific antigen is selected from the group consisting of lactate dehydrogenase-C and SP-10.

26. An avirulent microbe according to claim 1 wherein the gamete-specific antigen is an ovum-specific antigen.

27. An avirulent microbe according to claim 5 wherein the gamete-specific antigen is a sperm-specific antigen.

28. An avirulent microbe according to claim 5 wherein the sperm-specific antigen is selected from the group consisting of lactate dehydrogenase-C and SP-10.

29. An avirulent microbe according to claim 5 wherein the gamete-specific antigen is an ovum-specific antigen.

30. A vaccine composition comprising a therapeutically effective amount of an avirulent microbe according to claim 24, in combination with a pharmaceutically acceptable vehicle.

31. A vaccine composition comprising a therapeutically effective amount of an avirulent microbe according to claim 25, in combination with a pharmaceutically acceptable vehicle.

32. A vaccine composition comprising a therapeutically effective amount of an avirulent microbe according to claim 26, in combination with a pharmaceutically acceptable vehicle.

33. A vaccine composition comprising a therapeutically effective amount of an avirulent microbe according to claim 27, in combination with a pharmaceutically acceptable vehicle.

34. A vaccine composition comprising a therapeutically effective amount of an avirulent microbe according to claim 28, in combination with a pharmaceutically acceptable vehicle.

35. A vaccine composition comprising a therapeutically effective amount of an avirulent microbe according to claim 29, in combination with a pharmaceutically acceptable vehicle.

36. A method according to claim 16, wherein the gamete-specific antigen is a sperm-specific antigen.

37. A method according to claim 36, wherein the sperm-specific antigen is selected from the group consisting of lactate dehydrogenase-C and SP-10.

38. A method according to claim 16 wherein the gamete-specific antigen is an ovum-specific antigen.

39. A method according to claim 17, wherein the gamete-specific antigen is a sperm-specific antigen.

40. A method according to claim 17, wherein the sperm-specific antigen is selected from the group consisting of lactate dehydrogenase-C and SP-10.

41. A method according to claim 17 wherein the gamete-specific antigen is an ovum-specific antigen.

42. The avirulent microbe according to claim 1 wherein said avirulent microbe is capable of eliciting a mucosal immune response to lactic dehydrogenase-C.

43. The avirulent microbe according to claim 1 wherein said avirulent microbe is capable of eliciting a mucosal immune response to SP-10.

44. The avirulent microbe according to claim 1 wherein said avirulent microbe is capable of eliciting a mucosal immune response to ZP-3.

45. A vaccine composition comprising a therapeutically effective amount of an avirulent microbe according to claim 42.

46. A vaccine composition comprising a therapeutically effective amount of an avirulent microbe according to claim 43.

47. A vaccine composition comprising a therapeutically effective amount of an avirulent microbe according to claim 44.

48. A method for inducing an antifertility state in a vertebrate subject, said method comprising administering to said subject an effective amount of a vaccine composition according to claim 45.

49. A method for inducing an antifertility state in a vertebrate subject, said method comprising administering to said subject an effective amount of a vaccine composition according to claim 46.

50. A method for inducing an antifertility state in a vertebrate subject, said method comprising administering to said subject an effective amount of a vaccine composition according to claim 42.

L5 ANSWER 11 OF 11 USPATFULL
92:38305 Vaccines for the malaria circumsporozoite protein.
Brey, III, Robert N., Rochester, NY, United States
Majarian, William R., Pittsford, NY, United States
Pillai, Subramonia, Rochester, NY, United States
Hockmeyer, Wayne T., Pittsford, NY, United States
Praxis Biologics, Inc., Rochester, NY, United States (U.S. corporation)
US 5112749 19920512
APPLICATION: US 1987-104735 19871002 (7)
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is directed to attenuated strains of enteroinvasive bacteria that express a peptide or protein related to an epitope of the malaria parasites of the genus Plasmodium. The bacterial strains of the invention which can multiply in a host without causing significant disease or disorder, and which express a Plasmodium-related peptide that induces a protective immune response against malaria, can be used in live vaccine formulations for malaria. In specific embodiments, a Plasmodium-related peptide can be expressed as a fusion

protein, for example, with a bacterial enterotoxin.

The invention also relates to methods for expression of malaria antigens or fragments thereof within attenuated enteroinvasive bacteria.

In particular embodiments, the invention is directed to the expression by attenuated ***Salmonella*** spp. of epitopes of Plasmodium circumsporozoite proteins.

CLM What is claimed is:

1. An attenuated enteroinvasive bacterium of the genus ***Salmonella*** or Shigella comprising a recombinant DNA sequence which encodes an epitope of the circumsporozoite protein of a malaria parasite.

2. The recombinant bacterium of claim 1 wherein the bacterium is ***Salmonella*** typhi, ***Salmonella*** typhimurium or ***Salmonella*** enteritidis.

3. The bacterium of claim 2 which is selected from the group consisting of Ty21, Ty21a, Ty523 and Ty541.

4. The recombinant bacterium of claim 2 wherein the bacterium is a serotype dublin.

5. The bacterium of claim 1 wherein the epitope of the repeat region of the circumsporozoite protein.

6. The bacterium of claim 1 wherein the epitope is Region I or Region II of the circumsporozoite protein.

7. The bacterium of claim 1 wherein the recombinant DNA sequence encodes a fusion protein comprising an epitope of the circumsporozoite protein and the B-subunit of the heat-labile enterotoxin of E. coli or a portion thereof, such that said fusion protein is immunogenic.

8. The bacterium of claim 1 wherein the DNA sequence is expressed under the control of the lac operon promoter of E. coli, the tac promoter, the leftward promoter of bacteriophage lambda, or the rightward promoter of bacteriophage lambda.

9. The bacterium of claim 1 or 2 wherein the malaria parasite is Plasmodium falciparum.

10. The bacterium of claim 9 wherein the epitope comprises the amino acid sequence asn-ala-asn-pro.

11. The bacterium of claim 1 wherein the bacterium is ***Salmonella*** typhi ATCC accession number 67519.

12. The bacterium of claim 1 wherein the malaria parasite is Plasmodium vivax.

13. The bacterium of claim 1 wherein the malaria parasite is Plasmodium ovale.

14. The bacterium of claim 1 wherein the malaria parasite is Plasmodium malariae.

15. The bacterium of claim 1 wherein the malaria parasite is Plasmodium

berghei.

16. The bacterium of claim 15 wherein the epitope comprises the amino acid sequence asp-pro-ala-pro-pro-asn-ala-asn.

17. The bacterium of claim 1 wherein the bacterium is ***Salmonella*** enteriditis ATCC accession number 67521.

18. The bacterium of claim 1 wherein the bacterium is ***Salmonella*** enteritidis ATCC accession number 67520.

19. The bacterium of claim 1 wherein the malaria parasite is Plasmodium yoelii.

20. The bacterium of claim 1 wherein the malaria parasite is Plasmodium knowlesi.

21. The bacterium of claim 1 wherein the malaria parasite is Plasmodium cynomolgi.

22. A method of expressing an epitope of the circumsporozoite protein of a malaria parasite comprising: a. transforming an attenuated enteroinvasive bacterium of the genus ***Salmonella*** or Shigella with a vector comprising a recombinant DNA sequence which encodes an epitope of the circumsporozoite protein of a malaria parasite; and b. allowing the bacterium to grow under conditions which induce the expression of said circumsporozoite protein.

23. The method of according to claim 22 wherein the bacterium is ***Salmonella*** .

24. The method according to claim 23 wherein the bacterium is ***Salmonella*** typhi, ***Salmonella*** typhimurium or ***Salmonella*** enteritidis.

25. The method according to claim 22 wherein the DNA sequence is expressed under the control of the lac operon promoter of E. coli.

26. The method according to claim 23 wherein the DNA sequence is expressed under the control of the lac operon promoter of E. coli.

27. The method according to claim 26 wherein the bacterium is ***Salmonella*** typhi ATCC accession number 67519.

28. The method according to claim 22 wherein the DNA sequence is expressed under the control of the tac promoter.

29. The method according to claim 23 wherein the DNA sequence is expressed under the control of the tac promoter.

30. The method according to claim 29 wherein the bacterium is ***Salmonella*** enteritidis ATCC accession number 67521.

31. The method according to claim 22 wherein the DNA sequence is expressed under the control of the leftward promoter of bacteriophage lambda.

32. The method according to claim 23 wherein the DNA sequence is expressed under the control of the leftward promoter of bacteriophage

lambda.

33. The method according to claim 32 wherein the bacterium is ***Salmonella*** enteritidis ATCC accession number 67520.

34. The method according to claim 22 or 23 wherein the DNA sequence is expressed under the control of the rightward promoter of bacteriophage lambda.

35. The method according to claim 22 or 23 wherein the malaria parasite is Plasmodium falciparum.

36. The method according to claim 22 wherein the malaria parasite is Plasmodium vivax.

37. The method according to claim 22 wherein the malaria parasite is Plasmodium ovale.

38. The method according to claim 22 wherein the malaria parasite is Plasmodium malariae.

39. The method according to claim 22 or 23 wherein the malaria parasite is Plasmodium berghei.

40. The method according to claim 22 wherein the malaria parasite is Plasmodium yoelii.

41. The method according to claim 22 wherein the malaria parasite is Plasmodium knowlesi.

42. The method according to claim 22 wherein the malaria parasite is Plasmodium cynomolgi.

43. An attenuated enteroinvasive bacterium of the genus ***Salmonella*** or Shigella having an arcA or galE mutation and comprising a recombinant DNA sequence which encodes an epitope of the circumsporozoite protein of a malaria parasite.

44. The attenuated bacterium of claim 43, wherein the circumsporozoite protein is derived from Plasmodium falciparum.

45. The attenuated bacterium of claim 43, wherein the malaria parasite is Plasmodium berghei.

46. The attenuated bacterium of claim 43, wherein the recombinant DNA sequence encodes a fusion protein comprising an epitope of the circumsporozoite protein and the B-subunit of heat-labile enterotoxin of E. coli or a portion thereof, such that said fusion protein is immunogenic.

47. The attenuated bacterium of claim 46, wherein the fusion protein comprises the N-terminal 30 amino acids of the B subunit of the heat-labile enterotoxin of E. coli.

48. The attenuated bacterium of claim 46, wherein the bacterium is ***Salmonella*** typhi, ***Salmonella*** typhimurium, ***Salmonella*** dublin or ***Salmonella*** enteritidis.

49. The attenuated bacterium of claim 46, wherein the malaria parasite

is Plasmodium falciparum or Plasmodium vivax.

50. The attenuated bacterium of claim 46, wherein the malaria parasite is Plasmodium ovale, Plasmodium malariae, Plasmodium berghei, Plasmodium yoelii, Plasmodium knowlesi or Plasmodium cynomolgi.

L11 ANSWER 2 OF 7 USPATFULL
1998:108033 Vaccines containing a ***salmonella*** bacteria ***attenuated*** by mutation of the htra gene.
Dougan, Gordan, Beckenham, United Kingdom
Charles, Ian George, Beckenham, United Kingdom
Hormaeche, Carlos Estenio, Cambridge, United Kingdom
Johnson, Kevin Stuart, Cambridge, United Kingdom
Chatfield, Steven Neville, Beckenham, United Kingdom
Glaxo Wellcome Inc., Research Triangle Park, NC, United States (U.S. corporation)
US 5804194 19980908
APPLICATION: US 1994-350741 19941207 (8)
PRIORITY: GB 1990-7194 19900330
DOCUMENT TYPE: Utility.

AB Attenuated microorganism for use in immunoprophylaxis in which the attenuation is brought about by the presence of a mutation in the DNA sequence of the microorganism which encodes, or which regulates the expression of DNA encoding a protein that is produced in response to environmental stress, the microorganism optionally being capable of expressing DNA encoding a heterologous antigen.

CLM What is claimed is:
1. A vaccine comprising a prophylactically effective amount of a ***Salmonella*** bacterium ***attenuated*** by a non-reverting mutation in the htrA gene and a pharmaceutically acceptable carrier.

2. The vaccine as claimed in claim 1, wherein the mutation is a deletion mutation.

3. The vaccine as claimed in claim 1, wherein the mutation is an insertion mutation.

4. The vaccine as claimed in claim 1, wherein the bacterium is selected from the group consisting of Salmonella typhi, Salmonella typhimurium, Salmonella enteritidis and Salmonella cholerasuis.

5. The vaccine as claimed in claim 1, wherein the bacterium is further ***attenuated*** by a mutation in a second gene.

6. The vaccine as claimed in claim 5, wherein the mutation in a second gene is in a gene of the aromatic amino acid biosynthetic pathway.

7. The vaccine as claimed in claim 6, wherein the gene of the aromatic amino acid biosynthetic pathway is selected from the group consisting of aroC, aroA and aroD.

8. The vaccine as claimed in claim 1, wherein the bacterium expresses DNA encoding a heterologous antigen.

9. The vaccine as claimed in claim 1 in capsular form.

10. The method of prophylactic treatment of a host for an infection caused by Salmonella which comprises administering to said host a prophylactically effective dose of a ***Salmonella*** bacterium

attenuated by a non-reverting mutation in the htrA gene.

11. The method as claimed in claim 10, wherein the mutation is a deletion mutation.

12. The method as claimed in claim 10, wherein the mutation is an insertion mutation.

13. The method as claimed in claim 10, wherein the bacterium is selected from the group consisting of Salmonella typhi, Salmonella typhimurium, Salmonella enteritidis and Salmonella cholerasuis.

14. The method as claimed in claim 10, wherein said bacterium is further ***attenuated*** by a mutation in a second gene.

15. The method as claimed in claim 14, wherein the mutation in a second gene is in a gene of the aromatic amino acid biosynthetic pathway.

16. The method as claimed in claim 15, wherein the gene of the aromatic amino acid biosynthetic pathway is selected from the group consisting of aroC, aroA and aroD.

17. The method as claimed in claim 10, wherein the bacterium expresses DNA encoding a heterologous antigen.

18. The method as claimed in claim 10, wherein the bacterium is administered orally.

L11 ANSWER 3 OF 7 USPATFULL
1998:72257 Vaccines containing ***salmonella*** bacteria ***attenuated*** by mutations in two genes of the aromatic amino acid biosynthetic pathway.
Dougan, Gordon, Beckenham, United Kingdom
Chatfield, Steven Neville, Beckenham, United Kingdom
Hormaeche, Carlos Estenio, Cambridge, United Kingdom
Glaxo Wellcome, Inc., Research Triangle Park, NC, United States (U.S. corporation)
US 5770214 19980623
APPLICATION: US 1995-484314 19950607 (8)
PRIORITY: GB 1987-30037 19871223
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB An attenuated microorganism harbouring two mutated genes, each of which is located in the organisms aromatic pathway is provided. These organisms can usefully form the basis of a vaccine. They can be genetically engineered so as to express antigens from other pathogens and thus form the basis of a range of multi-valent vaccines.
CLM What is claimed is:
1. A vaccine comprising a pharmaceutically acceptable excipient and a Salmonella bacterium which is sufficiently ***attenuated*** such that it fails to cause a disease caused by the unattenuated bacterium, but which induces immunity in a mammal inoculated with the bacterium and provides protection against subsequent challenge with a virulent bacterium, wherein ***attenuation*** is attributable to a defined, non-reverting mutation in each of two discrete aro genes of the aromatic amino acid biosynthetic pathway selected from the group consisting of aroA, aroC, aroD and aroE.

2. A vaccine as claimed in claim 1 wherein the bacterium is Salmonella

typhi.

3. A vaccine as claimed in claim 1 wherein the ***attenuated*** bacterium expresses a heterologous antigen.

4. A vaccine as claimed in claim 3 wherein the ***attenuated*** bacterium contains an expression cassette having a DNA sequence encoding an antigen of a pathogen.

5. A vaccine as claimed in claim 1 adapted for oral administration.

6. A vaccine as claimed in claim 1 wherein the bacterium has no uncharacterized mutations in the genome thereof.

7. A vaccine as claimed in claim 1 which induces immunity in a human inoculated with the vaccine.

8. A method of effecting the prophylactic treatment of an infection by a pathogen, which method comprises administering to a mammal in need of said treatment an effective amount of a Salmonella bacterium which is sufficiently ***attenuated*** such that it fails to cause a disease caused by the unattenuated bacterium, but which induces immunity in the mammal and provides protection against subsequent challenge with the pathogen, wherein ***attenuation*** is attributable to a defined, non-reverting mutation in each of two discrete aro genes of the aromatic amino acid biosynthetic pathway selected from the group consisting of aroA, aroC, aroD and aroE.

9. A method as claimed in claim 8 wherein the bacterium is Salmonella typhi.

10. A method as claimed in claim 8 wherein the bacterium has no uncharacterized mutations in the genome thereof.

11. A method as claimed in claim 8 wherein the mammal is a human.

12. A method as claimed in claim 8 wherein the Salmonella bacterium expresses an antigen of the pathogen from an expression cassette having a DNA sequence encoding the antigen.

L11 ANSWER 4 OF 7 USPATFULL
97:101463 Expression of recombinant proteins in attenuated bacteria.
Charles, Ian George, Kent, England
Chatfield, Steven Neville, Kent, England
Fairweather, Neil Fraser, Kent, England
Glaxo Wellcome Inc., Research Triangle Park, NC, United States (U.S. corporation)
US 5683700 19971104
APPLICATION: US 1995-469507 19950606 (8)
PRIORITY: GB 1991-4596 19910305
GB 1991-21208 19911004
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns a method of prophylactically treating a host against infection by a microorganism, which method comprises administering to the host an attenuated Salmonella bacterium which contains a nirB promoter operably linked to a DNA sequence encoding a heterologous protein. The heterologous protein is expressed in the host

and induces in the host an immune response against the microorganism.

CLM What is claimed is:

1. A method for prophylactically treating a host against infection by a microorganism, which method comprises administering to the host an ***attenuated*** Salmonella bacterium which contains a nirB promoter operably linked to a DNA sequence encoding a heterologous protein, wherein the heterologous protein is expressed in the host and induces in the host an immune response against the microorganism.

2. The method according to claim 1, wherein the bacterium is selected from the group consisting of Salmonella typhi and Salmonella typhimurium.

3. The method according to claim 1, wherein ***attenuation*** of the bacterium is attributable to a non-reverting mutation in a gene in an aromatic amino acid biosynthetic pathway.

4. The method according to claim 3, wherein the bacterium harbours a non-reverting mutation in each of two discrete genes in the aromatic amino acid biosynthetic pathway.

5. The method according to claim 4, wherein the bacterium is selected from the group consisting of aroA aroC, AroA aroD and aroA aroE mutants.

6. The method according to claim 1, wherein the heterologous protein comprises an antigenic sequence from an organism selected from the group consisting of viruses, bacteria, fungi, yeasts and parasites.

7. The method according to claim 6, wherein the heterologous protein is selected from the group consisting of the P.69 protein from Bordetella pertussis and tetanus toxin fragment C.

L11 ANSWER 6 OF 7 USPATFULL
96:75115 Expression of recombinant proteins in attenuated bacteria.
Charles, Ian G., Kent, England
Chatfield, Steven N., Kent, England
Fairweather, Neil F., Kent, England
Burroughs Wellcome Co., Research Triangle Park, NC, United States (U.S. corporation)
US 5547664 19960820
APPLICATION: US 1994-354776 19941212 (8)
PRIORITY: GB 1991-4596 19910305
GB 1991-21208 19911004
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention concerns a vaccine comprising an attenuated Salmonella bacterium which contains a nirB promoter operably linked to a DNA sequence encoding a heterologous protein. The nirB promoter directs expression of the heterologous protein in a host it is wished to vaccinate.

CLM What is claimed is:

1. A vaccine comprising a pharmaceutically acceptable carrier or diluent and, as active ingredient, an ***attenuated*** Salmonella bacterium which contains a nirB promoter operably linked to a DNA sequence encoding a heterologous protein.

2. The vaccine according to claim 1, wherein the bacterium is selected from the group consisting of Salmonella typhi and Salmonella

typhimurium.

3. The vaccine according to claim 1, wherein the bacterium is ***attenuated*** due to a non-reverting mutation in a gene in an aromatic amino acid biosynthetic pathway.

4. The vaccine according to claim 3, wherein the bacterium harbours a non-reverting mutation in each of two discrete genes in the aromatic amino acid biosynthetic pathway.

5. The vaccine according to claim 4, wherein the bacterium is selected from the group consisting of aroA aroC, aroA aroD and aroA aroE mutants.

6. The vaccine according to claim 1, wherein the heterologous protein comprises an antigenic sequence from an organism selected from the group consisting of viruses, bacteria, fungi, yeasts and parasites.

7. The vaccine according to claim 6, wherein the heterologous protein is selected from the group consisting of the P.69 protein from Borderella pertussis and tetanus toxin fragment C.

L12 ANSWER 1 OF 3 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1999-494216 [41] WPIDS
DNC C1999-144832
TI A live vaccine for human immunodeficiency virus.
DC B04 D16
IN BURNETT, M S; ***KITTO, G B***
PA (RERE-N) RES DEV FOUND
CYC 84
PI WO 9939735 A1 19990812 (199941)* EN 74p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW
AU 9931801 A 19990823 (200005)
ZA 9900912 A 20000927 (200050) 69p
ADT WO 9939735 A1 WO 1999-US2503 19990204; AU 9931801 A AU 1999-31801 19990204; ZA 9900912 A ZA 1999-912 19990205
FDT AU 9931801 A Based on WO 9939735
PRAI US 1998-73943 19980206
AB WO 9939735 A UPAB: 19991011
NOVELTY - A live vaccine (I) for human immunodeficiency virus (HIV) comprising a recombinant plasmid containing a gene required for expression on a bacterial surface fused to a gene encoding an HIV protein.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method (II) of initiating immune responses specific for human immunodeficiency virus antigens in an individual in need of such treatment comprising the step of administering the individual with (I).
USE - The vaccine is used to prevent or treat HIV in humans.
Dwg.0/14

L17 ANSWER 1 OF 9 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
TI Prokaryotic, anaerobically inducible FNR promoters, designated dmsA, and its derivatives, useful for controlling expression of proteins in vectors used as vaccines.
AB WO 200044405 A UPAB: 20000918
NOVELTY - A recombinant DNA promoter comprising the defined consensus

sequence (I), is new. The promoter is a prokaryotic, anaerobically inducible FNR (undefined) promoter, dmsA (or derivatives: dmsA2 and dmsA3).

DETAILED DESCRIPTION - A recombinant DNA promoter comprising the consensus sequence (I):

AAATTTGATATATATCAAAT-X-T (I)

X = A or T.

The promoter is a anaerobically inducible FNR (undefined) promoter, dmsA (or derivatives: dmsA2 and dmsA3). Protein expression driven by these promoters is tightly controlled by anaerobiosis and inhibited by nitrate.

INDEPENDENT CLAIMS are also included for the following:

(1) a method for inducing a therapeutic response in vivo in an animal host comprising administering to the host a live bacterium which contains an anaerobically inducible prokaryotic promoter selected from dmsA, dmsA2 and/or dmsA3 (or derivatives) operably linked to a DNA sequence encoding a therapeutic protein;

(2) a therapeutic vector for administration to an animal host comprising a live bacterium which contains an anaerobically inducible prokaryotic promoter selected from dmsA, dmsA2 and/or dmsA3 (or derivatives) operably linked to a DNA sequence encoding a therapeutic protein;

(3) an independently functioning expression cassette comprising:

(a) an origin of replication;

(b) a promoter, the expression of which is anaerobically inducible; and

(c) the nucleic acid sequence of a desired product, the transcription of which is controlled by the promoter;

(4) an amplified plasmid replicon comprising the expression cassette of (4); and

(5) a bacterial cell comprising the amplified plasmid replicon of (5).

USE - The dmsA promoter may be used for in vivo expression of foreign genes, especially vaccine antigens, in live attenuated vaccine strains.

ADVANTAGE - The derivatives of dmsA are engineered to enhance gene expression under anaerobic growth conditions by optimizing the FNR binding sequence. The use of a dmsA promoter derivative for expression of foreign genes in live attenuated vaccines offers a modular promoter system for expression of proteins at different levels. This allows tailoring an optimal expression system by matching the level of expression of a specific antigen gene while imposing minimal metabolic stress on the carrier strain.

Dwg.0/3

L17 ANSWER 2 OF 9 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD

TI Isolated polynucleotide encoding a Chlamydia polypeptide useful to treat, diagnose and prevent disease caused by Chlamydia infection.

AB WO 200024902 A UPAB: 20000624

NOVELTY - An isolated polynucleotide (N1) encoding a 98 kDa outer membrane protein of a strain of Chlamydia pneumoniae, is new.

DETAILED DESCRIPTION - An isolated polynucleotide (N1) has a nucleotide sequence which comprises:

(a) a defined nucleotide sequence (I) of 3050 base pairs or functional fragments of (I);

(b) a polynucleotide sequence encoding a polypeptide with a sequence at least 75% homologous to (II) which has a defined protein sequence of 931 amino acids, or functional fragments; or

(c) a sequence capable of hybridizing under stringent conditions to a sequence comprising (I), or functional fragments.

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polypeptide (P1) with a sequence at least 75% homologous to (II), or functional fragments of (II);

(2) a polypeptide P2 comprising P1 linked to a fusion polypeptide;

(3) an expression cassette comprising N1 operably linked to a promoter;

(4) an expression vector comprising the expression cassette of (3);

(5) a host cell comprising the expression cassette of (3);

(6) a method of producing a recombinant polypeptide with sequence (II) comprising culturing the host cell of (5) and recovering the polypeptide;

(7) a ***vaccine*** ***vector*** comprising the expression cassette of (3);

(8) a pharmaceutical composition containing P1 and one or more known Chlamydia antigens;

(9) a method for inducing an immune response in a mammal comprising administering the ***vaccine*** ***vector*** of (7) or a composition containing P1 to induce an immune response;

(10) a polynucleotide probe reagent capable of detecting the presence of Chlamydia in biological material comprising a polynucleotide that hybridizes to N1 under stringent conditions;

(11) a hybridization method for detecting the presence of Chlamydia in a sample comprising:

(a) obtaining polynucleotide from the sample;

(b) hybridizing the obtained polynucleotide with the polynucleotide probe reagent of (10) under conditions allowing hybridization of the probe and the sample; and

(c) detecting any hybridization occurring;

(12) an amplification method for detecting the presence of Chlamydia in a sample comprising:

(a) obtaining polynucleotide from the sample;

(b) amplifying the polynucleotide using one or more polynucleotide probe reagents of (10); and

(c) detecting the amplified polynucleotide;

(13) a method for detecting the presence of Chlamydia in a sample comprising contacting the sample with a detecting reagent that binds to P1 in the sample and detecting the formed complex;

(14) an affinity chromatography method for substantially purifying a polypeptide with sequence (II) comprises:

(a) contacting a sample containing (II) with a detecting reagent that binds to the polypeptide to form a complex;

(b) isolating the formed complex;

(c) dissociating the formed complex; and

(d) isolating the dissociated polypeptide; and

(15) an antibody that immunospecifically binds P1 or a fragment or derivative of the antibody containing its binding domain.

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - Vaccine.

Balb/c mice (7-9 weeks old) were immunized intramuscularly and intranasally with plasmid DNA containing the coding sequence of C. pneumoniae 98 kDa outer membrane protein gene. Control animals were given saline or the plasmid vector without the chlamydial gene. The intramuscular immunization comprised 100 micro g DNA in 50 micro l phosphate buffered saline (PBS) at 0, 3 and 6 weeks and the intranasal immunization comprised 50 micro g DNA in 50 micro l PBS at 0, 3 and 6 weeks. At week 8, immunized mice were inoculated intranasally with 5x105 inclusion forming units (IFU) of C. pneumoniae, strain AR39 in 100 micro l SPG (sucrose, glutamate, phosphate) buffer. Lungs were taken from the mice at day 9 post challenge and homogenized in SPG buffer, the homogenate was assayed for the presence of infectious chlamydia by inoculation onto

monolayers of susceptible cells After incubation the monolayers were fixed and immunoperoxidase stained for the presence of chlamydial inclusions using convalescent sera from rabbits infected with C. pneumoniae and metal-enhanced DAB (not defined) as a peroxidase substrate. Mice immunized with the plasmid containing the 98 kDa outer membrane protein gene had chlamydial lung titers less than 300000 IFU/lung at day 5 and less than 144000 at day 9 compared to 685240 IFU/lung at day 5 and 238080 at day 9 for the control mice immunized with saline.

USE - The polynucleotides and polypeptides can be used as a vaccine for humans to treat or prevent disease caused by Chlamydia infection and P1, N1 or an antibody to P1 can be used to diagnose a Chlamydia infection. Dwg.0/4

L17 ANSWER 3 OF 9 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
TI Isolated polynucleotide encoding a Chlamydia polypeptide useful to treat, diagnose and prevent disease caused by Chlamydia infection.
AB WO 200024901 A UPAB: 20000624
NOVELTY - An isolated polynucleotide (N1) encoding a lorf2 protein of a strain of Chlamydia pneumoniae, is new.

DETAILED DESCRIPTION - An isolated polynucleotide (N1) has a nucleotide sequence which comprises:

(a) a defined nucleotide sequence (I) of 1550 base pairs or functional fragments of (I);

(b) a nucleotide sequence encoding a polypeptide with a sequence at least 75% homologous to (II) which has a defined protein sequence of 422 amino acids, or functional fragments; or

(c) a sequence capable of hybridizing under stringent conditions to a sequence comprising (I), or functional fragments.

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polypeptide (P1) with a sequence at least 75% homologous to (II), or functional fragments of (II);

(2) a polypeptide P2 comprising P1 linked to a fusion polypeptide;

(3) an expression cassette comprising N1 operably linked to a promoter;

(4) an expression vector comprising the expression cassette of (3);

(5) a host cell comprising the expression cassette of (3);

(6) a method of producing a recombinant polypeptide with sequence (II) comprising culturing the host cell of (5) and recovering the polypeptide;

(7) a ***vaccine*** ***vector*** comprising the expression cassette of (3);

(8) a pharmaceutical composition containing P1 and one or more known Chlamydia antigens;

(9) a method for inducing an immune response in a mammal comprising administering the ***vaccine*** ***vector*** of (7) or a composition containing P1 to induce an immune response;

(10) a polynucleotide probe reagent capable of detecting the presence of Chlamydia in biological material comprising a polynucleotide that hybridizes to N1 under stringent conditions;

(11) a hybridization method for detecting the presence of Chlamydia in a sample comprising:

(a) obtaining polynucleotide from the sample;

(b) hybridizing the obtained polynucleotide with the polynucleotide probe reagent of (10) under conditions allowing hybridization of the probe and the sample; and

(c) detecting any hybridization occurring;

(12) an amplification method for detecting the presence of Chlamydia in a sample comprising:

(a) obtaining polynucleotide from the sample;

(b) amplifying the polynucleotide using one or more polynucleotide probe reagents of (10); and

(c) detecting the amplified polynucleotide;

(13) a method for detecting the presence of Chlamydia in a sample comprising contacting the sample with a detecting reagent that binds to P1 in the sample and detecting the formed complex;

(14) an affinity chromatography method for substantially purifying a polypeptide with sequence (II) comprises:

(a) contacting a sample containing (II) with a detecting reagent that binds to the polypeptide to form a complex;

(b) isolating the formed complex;

(c) dissociating the formed complex; and

(d) isolating the dissociated polypeptide; and

(15) an antibody that immunospecifically binds P1 or a fragment or derivative of the antibody containing its binding domain.

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - Vaccine.

Balb/c mice (7-9 weeks old) were immunized intramuscularly and intranasally with plasmid DNA containing the coding sequence of C. pneumoniae lorf2 gene. Control animals were given saline or the plasmid vector without the chlamydial gene. The intramuscular immunization comprised 100 micro g DNA in 50 micro l phosphate buffered saline (PBS) at 0, 3 and 6 weeks and the intranasal immunization comprised 50 micro g DNA in 50 micro l PBS at 0, 3 and 6 weeks. At week 8, immunized mice were inoculated intranasally with 5x105 inclusion forming units (IFU) of C. pneumoniae, strain AR39 in 100 micro l SPG (sucrose, glutamate, phosphate) buffer. Lungs were taken from the mice at day 9 post challenge and homogenized in SPG buffer, the homogenate was assayed for the presence of infectious chlamydia by inoculation onto monolayers of susceptible cells After incubation the monolayers were fixed and immunoperoxidase stained for the presence of chlamydial inclusions using convalescent sera from rabbits infected with C. pneumoniae and metal-enhanced DAB (not defined) as a peroxidase substrate. Mice immunized with the plasmid containing the lorf2 gene had an average chlamydial lung titer of 11050 IFU/lung compared to 111783 IFU/lung for the control mice immunized with saline.

USE - The polynucleotides and polypeptides can be used as a vaccine for humans to treat or prevent disease caused by Chlamydia infection and P1, N1 or an antibody to P1 can be used to diagnose a Chlamydia infection.

Dwg.0/4

L17 ANSWER 4 OF 9 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD

TI Novel antigens and corresponding DNA molecules that can be used to prevent, treat and diagnose disease caused by Chlamydia infection in mammals, especially humans.

AB WO 200011183 A UPAB: 20000419

NOVELTY - Isolated Chlamydia pneumoniae polypeptides (PP) encoded by one of the amino acid sequences of 147-970 amino acids (aa) (I)-(VIII) are new. All sequences are fully disclosed in the specification.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a polynucleotide (PN) encoding a (PP) having a sequence that is at least 75% homologous to and/or a functional fragment of the (aa) selected from (I)-(VIII), where the (PN) comprises one of the nucleotide sequences of 650-3200 base pairs (bp) (IX)-(XVI);

(2) (PP) encoded by one of the amino acid sequences of 147-970 amino acids (aa) (I)-(VIII) linked to a fusion polypeptide;

(3) an expression cassette comprising one of the nucleotide sequences of 650-3200 base pairs (bp) (IX)-(XVI) operably linked to a promoter;

(4) an expression vector comprising (3);

(5) a host cell comprising (3);
(6) producing a recombinant (PP), comprising:
(a) culturing (5), to allow expression of the (PP); and
(b) recovering the recombinant (PP);
(7) a ***vaccine*** ***vector*** comprising the (3);
(8) a (PN) probe reagent capable of detecting the presence of Chlamydia in biological material, comprising a (PN) that hybridizes to the (PN) that comprises one of the nucleotide sequences of 650-3200 base pairs (bp) (IX)-(XVI);
(9) a hybridization method for detecting the presence of Chlamydia in a sample, comprising:
(a) obtaining (PN) from the sample;
(b) hybridizing the (PN) of with (8); and
(c) detecting the hybridization of (8) with a (PN) in the sample;
(10) an amplification method for detecting the presence of Chalmydia in sample, comprising:
(a) see (9) (a);
(b) amplifying the (PN) using one or more (8); and
(c) detecting the amplified (PP) (sic);
(11) detecting the presence of Chlamydia in a sample comprising:
(a) contacting the sample with a detecting reagent that binds to a (PP) to form a complex (C), the (PP) being selected from the following: (CPN 100)111, 224, 230, 231, 232, 235, 394, and 395; and
(b) detecting (C);
(12) an affinity chromatography method for substantially purifying a Chlamydia antigen comprising:
(a) contacting a sample containing the Chalmydia antigen with a detecting reagent that binds to a (PP) to form a (C), the (PP) being selected from the (PP) in (11) (a);
(b) isolating (C);
(c) dissociating (C); and
(d) isolating the dissociated Chlamydia antigen; and
(13) an antibody (ab) immunospecific for (PP) encoded by one of the amino acid sequences of 147-970 amino acids (aa) (I)-(VIII), or a fragment or derivative of the (ab) containing the binding domain of the (ab).

ACTIVITY - Antibacterial; anti-pneumonia; antitussive; antiasthmatic. No biological data given.

MECHANISM OF ACTION - Vaccine. No biological data given.

USE - Isolated Chlamydia polypeptides (PP) may be used to prevent, treat and detect the presence of Chlamydia infection and/or the presence of Chlamydia in a sample. The (PP) encoded by one of the amino acid sequences of 147-970 amino acids (aa) (I)-(VIII) may be used to induce an immune response in a mammal. The vaccine vector comprising a polynucleotide (PN) where the (PN) comprises one of the nucleotide sequences of 650-3200 base pairs (bp) (IX)-(XVI) given in the specification is used to induce an immune response in a mammal. The (PN) probe is capable of detecting the presence of Chlamydia in biological material. (All claimed). The antibody may also be used therapeutically to treat and/or prevent a Chlamydia infection. The above compositions may also be used for veterinary treatment, for example, to treat and/or prevent Chlamydia infections in cats and dogs.

ADVANTAGE - There is increasing evidence that Chlamydia pneumoniae may be linked to other diseases/conditions including chronic bronchitis, asthma and sinusitis and can lead to hospitalization in patients with underlying illness, as well as non-respiratory diseases. Several studies have shown a correlation of previous infections with C.pneumoniae and heart attacks, coronary artery and carotid artery disease. (See, Fong et al., (1997) Journal of Clinical Microbiology 35:48). Therefore, the vaccine disclosed may have further indirect clinical applications and

concomitant advantages, for example, reducing the likelihood of heart disease while preventing C.pneumoniae infection (No biological data is given). Antibiotic resistance is increasingly common and the vaccine preparation provides an alternative method of treatment. Further, exposure to other Chlamydia.spp affords no cross-protection to C.pneumoniae infection.
Dwg.0/16

L17 ANSWER 5 OF 9 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
TI A new attenuated ***Salmonella*** useful as a vaccine against ***Salmonella*** , Shigella or E. coli.
AB WO 9945120 A UPAB: 19991103
NOVELTY - An attenuated ***Salmonella*** , having gene mutations that reduce enteropathogenicity of the organism, is new.

DETAILED DESCRIPTION - The attenuated ***Salmonella*** or other enteric bacteria, has reduced enteropathogenicity but substantially equal invasiveness compared to the wild-type, where:

(a) if ***Salmonella*** , has alteration(s) in sopA, sopD, sipA, and/or a gene from the pathogenicity island SPI5, where if the alteration is to SPI-5sopB it has another alteration in one of the above genes, or

(b) if another bacteria, has an alteration in homologous gene(s) corresponding to those in (a).

INDEPENDENT CLAIMS are also included for the following:

(1) a prophylactic or therapeutic medicament comprising one or more attenuated ***Salmonella*** ;

(2) a sopA, pipD, orfX, pipC, pipB or pipA polypeptide (P1) having one of the amino acid sequences fully defined in the specification, or a peptide (P2) comprising a characteristic part of that polypeptide;

(3) a P1 or P2 mutant, variant, derivative, functional mimetic or allele;

(4) a polypeptide having at least 20% homology to P1;

(5) a substance comprising the polypeptide of (2), (3) or (4) and another peptide sequence(s);

(6) a nucleic acid (N1) encoding (2), (3), (4) or (5);

(7) a vector comprising N1;

(8) a host cell transformed with the above vector;

(9) identifying a gene corresponding to a ***Salmonella*** sopA, pipD, orfX, pipC, pipB or pipA, comprising using N1 as a probe in a test sample, observing hybridization, and optionally isolating hybridized nucleic acid;

(10) an antibody, or antibody fragment, derivative, functional equivalent or homologue which binds P1 or N1;

(11) generating an attenuated ***Salmonella*** for use as a ***vaccine*** or ***vaccine*** ***vector*** , comprising:

(a) introducing a genomic mutation in sopA, sopD, sipA, and/or a gene from the pathogenicity island SPI5, where if the alteration is to SPI-5sopB another alteration is also introduced, and

(b) selecting and culturing a mutant which has reduced enteropathogenicity but substantially equal invasiveness compared to the wild-type;

(12) screening for an agent which modulates P1 or P2 activity, comprising contacting the candidate agent(s) with P1 or P2, and detecting a change in activity;

(13) an agent identified by the above method.

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - Vaccine.

USE - The medicament is used to treat or immunize against ***Salmonella*** , Shigella or E. coli infection, particularly in a person or agricultural animal, and to detect one of those organisms in a

sample (claimed). Strains of ***Salmonella*** include S. typhimurium, S. enteritidis, S. dublin and S. choleraesuis. N1 and the proteins it encodes are used as immunogens, in the production of monoclonal antibodies and in the detection of the above ***Salmonella*** strains. The substances of (1) to (5) and N1 can be used to screen for agents which affect or modulate their activity (all claimed).
Dwg.0/27

L17 ANSWER 6 OF 9 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
TI Oral contraceptive ***vaccine*** containing recombinant ***salmonella*** - transformed with ***vector*** containing gene for fertility control antigen.
AB DE 19720761 A UPAB: 19981223
Use of a vector for expression and secretion of a fertility control antigen in attenuated ***salmonella*** or other attenuated Gram-negative vaccine strains to produce an oral ***vaccine*** is new. The ***vector*** comprises a gene encoding the fertility control antigen under the control of a complete haemolysin operon, including the hly specific promoter and the hlyR enhancer-like regulator but excluding most of the hlyA gene.
USE - The vector is used for immunological contraception by oral administration.
Dwg.1/10

L17 ANSWER 7 OF 9 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
TI Inducing immune response to tumour-specific antigen in host with cancer - comprises administering recombinant Listeria monocytogenes expressing tumour-specific antigen or fragment.
AB WO 9614087 A UPAB: 19960625
Inducing an immune response to a tumour-specific antigen in a host with cancer comprises administering a vaccine contg. a recombinant form of Listeria monocytogenes (LM) expressing a tumour-specific antigen or fragment. Also claimed is a vaccine for inducing an immune response to a tumour-specific antigen comprising LM as above.
USE - The vaccine is useful to induce an immune response to a tumour-specific antigen and suppress tumour formation in a host, partic. leukaemia, melanoma, cervical, breast or pancreatic cancer (all claimed).
ADVANTAGE - The recombinant LM elicits a strong, antigen-specific cytotoxic T cell response in vivo, serving as an ideal ***vaccine*** ***vector*** for boosting this response to tumour-specific proteins and a unique system to prime the cellular immune response as a vaccine against cancer. The live vaccine results in a long-lasting cellular immunity, and due to the life cycle of LM, can target foreign proteins and fragments to the class I MHC restricted pathway. The vaccine is also safer than many other live vectors as LM is susceptible to most antibiotics, including penicillin. LM also lacks the problems associated with toxicity from enterotoxins which Gram-negative vectors, e.g. ***Salmonella*** sp., present. Pre-existing immunity which could prevent effective boosting by a vector already widely used as a vaccine is not a problem, as LM has not been used previously in vaccine development.
Dwg.0/8

L17 ANSWER 8 OF 9 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
TI Vaccine to protect pigs against swine dysentery - comprises treponema hyodysenteriae endo-flagellum sheath protein, applied orally or intranasally.
AB EP 534526 A UPAB: 19930924
Polynucleotide encodes all or part of the endoflagellum sheath protein of Treponema hyodysenteriae. Polynucleotide is obtd. from: (a) DNA having a

1140 bp sequence (given in specification), (b) polynucleotide which hybridises with (a) and which encodes a polypeptide with the immunogenic properties of the endoflagellum sheath protein of T.hyodysenteriae, and (c) polynucleotides which are degenerate as a result of the genetic code to (a) or (b), with the immunogenic properties of (b).

Also claimed is a polypeptide with all or some of the aminoacids of the endoflagellum sheath protein of T.hyodysenteriae; and a vaccine for combating T.hyodysenteriae infection comprising the above polypeptide.

The vaccine may also comprise other immunogens, e.g., pseudorabies, influenza, transmissible gastroenteritis, parvovirus, porcine endemic diarrhoea or hog cholera viruses, mycoplasmas, e.g., M.hyopneumoniae and M.lyorhinis, or bacteria such as E.coli, Bordetella bronchiseptica, Leptospira, Actinobacillus pleuropneumonia, Pasteurella multocida or Streptococcus suis.

USE/ADVANTAGE - To combat T.hyodysenteriae infections, esp. swine dysentery. The ***vaccine*** is esp. a bacterial ***vector*** vaccine, and the bacterium is ***salmonella*** . The vaccine is applied orally, intranasally or i.m.

0/9

L17 ANSWER 9 OF 9 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
TI New oral bivalent ***vaccine*** contg. avirulent ***Salmonella*** typhi - with ***vector*** whose DNA encodes LT-B of E coli, useful for preventing typhoid fever and cholera-like endotoxin-induced diarrhoeal disease.
AB US 5079165 A UPAB: 19931006
A stable avirulent strain of ***Salmonella*** typhi is claimed which contains an expression vector contg. DNA encoding the E. coli LT-B subunit of the heat-labile enterotoxin of pJC217. Also claimed is a pharmaceutical compsn. comprising a stable avirulent strain of S. typhi of (A) contg. DNA coding for the non-toxic polypeptide of the LT-B subunit of the heat-labile enterotoxin of E. coli that is replicated, transcribed and translated, and a carrier.

The LT-B gene was isolated from E. coli and cloned into pBR322 then PUC 8 to obtain pJC217. The pJC217 was used to transform a streptomycin resistant mutant of S.typhi strain Ty21a to obtain S. typhi SE12, ATCC 39842.

USE/ADVANTAGE - The modified S. typhi can be used as an oral bivalent vaccine to provide protection against both typhoid fever and cholera-like enterotoxin-induced diarrhoeal disease.

0/4

L21 ANSWER 1 OF 7 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 2000-293149 [25] WPIDS
DNC C2000-088672
TI Isolated outer membrane protein from a Moraxella catarrhalis strain used for diagnosis treatment and prevention of disease caused by M. catarrhalis e.g. pneumonia, otitis media and respiratory infections.
DC B04 D16
IN TILLMANN, U F; TUCKER, K
PA (ANTE-N) ANTEX BIOLOGICS INC
CYC 87
PI WO 2000018910 A1 20000406 (200025)* EN 108p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW

AU 9964100 A 20000417 (200035)
ADT WO 2000018910 A1 WO 1999-US22918 19991001; AU 9964100 A AU 1999-64100 19991001
FDT AU 9964100 A Based on WO 200018910
PRAI US 1998-164714 19981001
AB WO 200018910 A UPAB: 20000524
NOVELTY - An isolated or substantially purified outer membrane protein (OMP), OMP21, from a Moraxella catarrhalis strain with an apparent molecular weight of 16-20 kD as determined by sodium dodecylsulfate polyacrylamide gel electrophoresis (SDS-PAGE), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a peptide fragment of OMP21 which specifically binds to an antibody that specifically binds OMP21;

(2) an isolated nucleic acid molecule (I) encoding OMP21, a complementary sequence, a sequence substantially homologous to, or any fragment of OMP21;

(3) plasmid pOMP21X obtainable from Escherichia coli Top10F' (pOMP21X) deposited as ATCC 98878;

(4) a recombinant ***expression*** ***vector*** (II) adapted for transformation of a host cell comprising (I) or the plasmid of (3);

(5) a recombinant ***expression*** ***vector*** (III) adapted for transformation of a host cell comprising (I) and an expression system operatively coupled to a nucleic acid molecule for expression by the host of OMP21;

(6) a transformed host cell containing (II) or (III);

(7) an isolated recombinant OMP21 producible by the transformed host cell of (6);

(8) an ***attenuated*** or inactivated cultivar of M. catarrhalis where the cultivar has been genetically manipulated to delete the nucleic acid encoding OMP21 so it is non-transcribed;

(9) a pharmaceutical composition which is prophylactic, therapeutic, or immunogenic including a vaccine, or a vaccine comprising at least one component selected from:
(a) OMP21;
(b) (I);

(c) OMP21, obtained from a transformed host comprising an ***expression*** ***vector*** containing (I) and a means of expression coupled to the nucleic acid for expression of OMP21 by the host;

(d) a recombinant vector comprising (I); and

(e) a transformed cell comprising the vector of (d);

(10) antisera raised against the compositions or vaccine of (9);

(11) an isolated antibody (IV) present in the antisera of (10) that specifically binds one or more of the components present in the compositions or vaccine of (9);

(12) a method for detecting anti-M. catarrhalis antibodies in a test sample comprising:

(a) contacting a test sample with the composition of (9) in the presence of anti-M. catarrhalis antibodies to form antigen:anti-M. catarrhalis antibody immunocomplexes; and

(b) detecting any immunocomplexes formed as an indication of the presence of anti-M. catarrhalis antibodies in the test sample;

(13) a diagnostic kit for detecting antibodies to M. catarrhalis comprising the pharmaceutical compositions of (9), a container and a reagent for detecting M. catarrhalis antigen:anti-M. catarrhalis antibody immunocomplexes formed between the compositions and the sample;

(14) a method for detecting the presence of M. catarrhalis in a test sample comprising contacting a test sample with the antibodies of (11) and

detecting any immunocomplexes formed as an indication of the presence of M. catarrhalis in the test sample;

(15) a diagnostic kit for detecting the presence of M. catarrhalis comprising the antibodies of (11), a container and a reagent for measuring M. catarrhalis:anti-M. catarrhalis antibody immunocomplexes formed between the antibodies and M. catarrhalis;

(16) a method for determining the presence of nucleic acid encoding OMP21 in a sample comprising contacting a sample with (I) to produce duplexes comprising (I) and any nucleic acid molecule encoding OMP21 in the sample specifically hybridizable with (I) and detecting the duplexes produced;

(17) a diagnostic kit for determining the presence of nucleic acid encoding OMP21 in a sample comprising (I), a device for contacting (I) with a test sample and a device for detecting duplexes produced; and

(18) a method of preventing, treating or ameliorating a disorder related to M. catarrhalis in an animal in need of treatment comprising administering an effective amount of the compositions or vaccine of (9).

ACTIVITY - Antibacterial; auditory; antiinflammatory.

MECHANISM OF ACTION - Vaccine.

Pre-immune serum and anti-OMP21 antiserum was examined for activity in mediating complement killing of M. catarrhalis using the Serum Bactericidal Test described by Zollinger et al in Immune responses to Neisseria meningitis, Manual of Clinical Laboratory Immunology, 3rd ed., 347-349 with cells of M. catarrhalis strains not N. meningitis cells. The anti-OMP21 antiserum mediated complement-killing of M. catarrhalis ATCC 49143 but not of a deletion mutant of M. catarrhalis with the OMP21 gene disrupted.

USE - OMP21, its nucleic acids and antibodies can be used in prophylactic and therapeutic compositions for treating a M. catarrhalis bacterial infection, otitis media, respiratory infections, sinusitis and pneumonia (claimed). They are useful as reagents for the clinical or medical diagnosis of M. catarrhalis infections and for scientific research on the properties of pathogenicity, virulence and infectivity of M. catarrhalis and host defense mechanisms.

The antibodies, particularly those that are cytotoxic may be used in passive immunization to prevent or attenuate M. catarrhalis infections of animals e.g. humans.

Dwg.0/9

L21 ANSWER 2 OF 7 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1998-609995 [51] WPIDS
DNC C1998-182827
TI ***Attenuated*** ***Salmonella*** strain carrying eukaryotic vectors expressing heterologous/autologous genes - can be used for oral, nasal or mucosal vaccines in gene delivery to vertebrates.
DC B04 D16
IN CHAKRABORTY, T; DARJI, A; GERSTEL, B; GUZMN, C; TIMMIS, K; WACHHOLZ, P; WEHLAND, J; WEISS, S; GUZM, N C; GUZMAN, C
PA (GBFB) GES BIOTECHNOLOGISCHE FORSCHUNG MBH
CYC 74
PI WO 9848026 A1 19981029 (199851)* EN 52p
RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN
AU 9857562 A 19981113 (199913)
EP 977874 A1 20000209 (200012) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

ADT WO 9848026 A1 WO 1997-EP6933 19971211; AU 9857562 A AU 1998-57562 19971211; EP 977874 A1 EP 1997-953786 19971211, WO 1997-EP6933 19971211
FDT AU 9857562 A Based on WO 9848026; EP 977874 A1 Based on WO 9848026
PRAI EP 1997-106503 19970418
AB WO 9848026 A UPAB: 19981223
New ***attenuated*** ***Salmonella*** strain carries a eukaryotic vector for expressing a heterologous/autologous gene or gene fragment within an open reading frame inside the vector. The ***attenuation*** is adjusted to the vaccination of vertebrates including humans.
Also claimed are:
(1) a recovery process for the ***attenuated*** ***Salmonella*** strain ;
(2) a vaccine for oral and/or nasal gene delivery comprising the ***Salmonella*** strain; and
(3) an immunogenic protein or protective antigen expressed by the vector, where: (a) a gene or gene fragment from a heterologous/autologous DNA/cDNA library is expressed by a eukaryotic ***expression*** ***vector*** carried by an ***attenuated*** ***Salmonella*** strain; (b) a DNA vaccination is performed using the ***Salmonella*** strain; (c) screening for an expressed product is performed according to (a) providing an immune response; and (d) recovery of a ***Salmonella*** strain, immunogenic protein or protective antigen is performed.
USE - The strain can be used to form a vaccine for oral/nasal/mucosal gene delivery to vertebrates, especially humans. The strain together with vaccine can be used for expression screening of heterologous genomic DNA libraries or genomic cDNA libraries through vaccination.
ADVANTAGE - The use of ***attenuated*** ***Salmonella*** carrying eukaryotic expression vectors enables genetic immunisation by oral administration of the carrier. Also, a very versatile system for new immunisation strategies is provided by the stimulation of cytotoxic/helper T cells and the induction of a strong antigen response. The method enables the possibility of genetic immunisation with DNA fragments containing open reading frames, which define the function of new gene products, provide novel serological reagents, allow delineation and assess efficiencies of protective antigens in vaccination protocols.
Dwg.0/13

L21 ANSWER 3 OF 7 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1998-437476 [37] WPIDS
DNC C1998-133109
TI New non-functional mutant nucleic acid from ***Salmonella*** msbB or htrB genes - and recombinant microorganisms containing them, producing lipid A of reduced, or zero, toxicity, useful as live ***attenuated*** vaccines.
DC B04 D16
IN DOUGAN, G; MASKELL, D J
PA (UNLO) IMPERIAL COLLEGE SCI TECHNOLOGY & MED
CYC 80
PI WO 9833923 A1 19980806 (199837)* EN 38p
RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN
AU 9858734 A 19980825 (199903)
EP 973911 A1 20000126 (200010) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI NL PT SE
ADT WO 9833923 A1 WO 1998-GB291 19980130; AU 9858734 A AU 1998-58734 19980130;

EP 973911 A1 EP 1998-902105 19980130, WO 1998-GB291 19980130
FDT AU 9858734 A Based on WO 9833923; EP 973911 A1 Based on WO 9833923
PRAI GB 1997-1887 19970130; GB 1997-1886 19970130
AB WO 9833923 A UPAB: 19980916
Nucleic acid (I) from a mutant msbB or htrB gene, derivable from ***Salmonella*** , that results in loss of msbB- or hrtB-encoded protein (II), or loss of function of (II), in turn resulting in a lipid A molecule of reduced toxicity, is new. Also claimed are: (1) polypeptides (III) encoded by (I); (2) recombinant DNA construct containing (I), particularly in cloning or ***expression*** ***vector*** ; (3) recombinant microorganism containing this construct; (4) microorganism that contains (I) for one or both of msbB and htrB, or in which one or both of these genes is inactivated or absent; (5) a microorganism having the characteristics of NCIMB deposit number 40856.

USE - Microorganisms of (4) are used as live (***attenuated*** or ***avirulent***) vaccines to protect against infection by the corresponding wild type, in humans, other mammals or birds. They can also be used (not claimed) for production of nucleic acid or protein for therapeutic use, e.g. lipopolysaccharides (LPS) produced by them are useful as endotoxin antagonists, typically lipid IVa-KDO2 for treatment of septic shock

ADVANTAGE - The new microorganisms have reduced endotoxicity and thus reactogenicity, but are still viable and can be cultured without addition of supplements. When used for nucleic acid/protein production, they eliminate the need for removal of toxic LPS.

Dwg.1/6

L21 ANSWER 4 OF 7 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1994-065703 [08] WPIDS
CR 1995-082234 [11]
DNC C1994-029543
TI DNA construct comprising environmentally-induced promoter and DNA encoding two proteins linked by hinge region - pref. tetanus toxin C to enhance immunogenicity of second antigenic protein in transformed ***Salmonella*** , used in vaccines.
DC B04 D16
IN CHATFIELD, S N; DOUGAN, G; HORMAECHE, C E; KHAN, M A; VILLARREAL-RAMOS, B; CHATFIELD, S; HORMAECHE, C; KHAN, M
PA (MEDE-N) MEDEVA HOLDINGS BV
CYC 44
PI WO 9403615 A1 19940217 (199408)* EN 89p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
W: AT AU BB BG BR BY CA CH CZ DE DK ES FI GB HU JP KP KR KZ LK LU MG MN MW NL NO NZ PL PT RO RU SD SE SK UA US
AU 9347193 A 19940303 (199426)
FI 9500396 A 19950130 (199516)
NO 9500348 A 19950328 (199523)
EP 652962 A1 19950517 (199524) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
JP 08503602 W 19960423 (199645) 80p
EP 863211 A1 19980909 (199840) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
EP 652962 B1 19981216 (199903) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
DE 69322645 E 19990128 (199910)
ES 2127829 T3 19990501 (199924)
ADT WO 9403615 A1 WO 1993-GB1617 19930730; AU 9347193 A AU 1993-47193 19930730; FI 9500396 A WO 1993-GB1617 19930730, FI 1995-396 19950130; NO 9500348 A WO 1993-GB1617 19930730, NO 1995-348 19950130; EP 652962 A1 EP

1993-917957 19930730, WO 1993-GB1617 19930730; JP 08503602 W WO 1993-GB1617 19930730, JP 1994-505102 19930730; EP 863211 A1 Div ex EP 1993-917957 19930730, EP 1998-104783 19930730; EP 652962 B1 EP 1993-917957 19930730, WO 1993-GB1617 19930730, Related to EP 1998-104783 19930730; DE 69322645 E DE 1993-622645 19930730, EP 1993-917957 19930730, WO 1993-GB1617 19930730; ES 2127829 T3 EP 1993-917957 19930730

FDT AU 9347193 A Based on WO 9403615; EP 652962 A1 Based on WO 9403615; JP 08503602 W Based on WO 9403615; EP 863211 A1 Div ex EP 652962; EP 652962 B1 Related to EP 863211, Based on WO 9403615; DE 69322645 E Based on EP 652962, Based on WO 9403615; ES 2127829 T3 Based on EP 652962

PRAI GB 1993-6398 19930326; GB 1992-16317 19920731

AB WO 9403615 A UPAB: 19981021

DNA construct comprises a promoter sequence operably linked to a DNA sequence encoding first and second proteins linked by a hinge region, where the promoter has activity which is induced in response to a change in the surrounding environment. Also claimed are: a replicable ***expression*** ***vector*** , suitable for use in bacteria, contg. the construct; a bacterium transformed with this vector; and a fusion protein comprising tetanus toxin fragment C or 1 or more of its epitopes, linked to a heterologous protein.

USE/ADVANTAGE - The first and second proteins are antigenic sequences derived from viruses, bacteria, fungi, yeasts or parasites. The first sequence is pref. tetanus toxin C or epitopes, known to have potent immunogenicity in ***Salmonella*** . These proteins can be used in the prepn. of vaccines against the pathogens. Such vaccines may comprise ***attenuated*** bacteria expressing these proteins, pref. double aro mutants of S. typhi or S. typhimurium. The flexible hinge region between the antigenic regions of the fusion protein allows protein formation to be maintained.

Dwg.0/14

L21 ANSWER 5 OF 7 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD

AN 1992-331734 [40] WPIDS

CR 1992-331735 [40]

DNC C1992-147533

TI Expression of heterologous protein - by using a promoter inducible by anaerobic conditions.

DC B04 D16

IN CHARLES, I G; COLE, J A; MAKOFF, A J; OXER, M; PEAKMAN, T C

PA (WELL) WELLCOME FOUND LTD; (WELL) BURROUGHS WELLCOME CO

CYC 23

PI WO 9215688 A1 19920917 (199240)* EN 22p
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE
W: JP US
NO 9302423 A 19930702 (199341)
FI 9303757 A 19930826 (199345)
EP 574466 A1 19931222 (199351) EN
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL
CZ 9301005 A3 19940119 (199410)
SK 9300555 A3 19931006 (199420)
JP 06505158 W 19940616 (199428) 10p
HU 66833 T 19950130 (199510)
US 5547664 A 19960820 (199639) 10p
RU 2126447 C1 19990220 (200022)

ADT WO 9215688 A1 WO 1992-GB386 19920305; NO 9302423 A WO 1992-GB387 19920305, NO 1993-2423 19930702; FI 9303757 A WO 1992-GB387 19920305, FI 1993-3757 19930826; EP 574466 A1 EP 1992-905914 19920305, WO 1992-GB387 19920305; CZ 9301005 A3 CZ 1993-1005 19920305; SK 9300555 A3 SK 1993-555 19930514; JP 06505158 W JP 1992-505563 19920305, WO 1992-GB387 19920305; HU 66833 T WO

1992-GB387 19920305, HU 1993-2492 19920305; US 5547664 A Cont of WO 1992-GB387 19920305, Cont of US 1993-81361 19930630, Cont of US 1994-246773 19940520, US 1994-354776 19941212; RU 2126447 C1 WO 1992-GB387 19920305, RU 1993-57957 19920305

FDT EP 574466 A1 Based on WO 9215689; JP 06505158 W Based on WO 9215689; HU 66833 T Based on WO 9215689

PRAI GB 1991-4596 19910305; GB 1991-21208 19911004; WO 1992-GB387 19920305

AB WO 9215688 A UPAB: 20000508

Process comprises maintaining under anaerobic conditions bacteria in which the expression of the protein is under the control of a promoter whose activity is induced by anaerobic conditions. The promoter is pref. nirB promoter.

Also claimed are: (A) a replicable ***expression*** ***vector*** , suitable for use in bacteria, in which a DNA sequence encoding a heterologous protein is under the control of a promoter whose activity is induced by anaerobic conditions; and (B) use of a promoter activated by anaerobic condtions for the control of expression of a heterologous protein in bacteria.

USE/ADVANTAGE - The transformed bacteria are able to express heterologous genes very efficiently, partic. in the case of large scale fermentation involving high cell densities, in the absence of oxygen. The aerobic conditions required during the growth phase can be readily maintained allowing high biomass to be achieved prior to induction

Dwg.0/2

L21 ANSWER 6 OF 7 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD

AN 1990-334550 [44] WPIDS

DNC C1990-145200

TI ***Avirulent*** phoP ***salmonella*** mutants - used to prepare vaccines against disease caused by ***salmonella*** or other pathogenic microorganisms.

DC B04 D16

IN CURTISS, R; GALAN, J; ROY, C

PA (UNIW) UNIV WASHINGTON

CYC 17

PI WO 9011687 A 19901018 (199044)* 68p
RW: AT BE CH DE DK ES FR GB IT LU NL SE
CA 2013573 A 19900930 (199051)
AU 9053560 A 19901105 (199105)
EP 465560 A 19920115 (199203)
R: AT BE CH DE ES FR GB IT LI LU NL SE
JP 04504204 W 19920730 (199237) 20p
AU 645489 B 19940120 (199409)
EP 465560 A4 19920408 (199521)
US 5424065 A 19950613 (199529) 18p
EP 465560 B1 19960605 (199627) EN 29p
R: AT BE CH DE DK ES FR GB IT LI LU NL SE
DE 69027313 E 19960711 (199633)
ES 2090129 T3 19961016 (199647)
CA 2013573 C 19990119 (199914)
JP 3004049 B2 20000131 (200010) 29p

ADT EP 465560 A EP 1990-905859 19900323; JP 04504204 W JP 1990-505536 19900323, WO 1990-US1573 19900323; AU 645489 B AU 1990-53560 19900323; EP 465560 A4 EP 1990-905859 ; US 5424065 A Cont of US 1989-331979 19890331, US 1992-981935 19921119; EP 465560 B1 EP 1990-905859 19900323, WO 1990-US1573 19900323; DE 69027313 E DE 1990-627313 19900323, EP 1990-905859 19900323, WO 1990-US1573 19900323; ES 2090129 T3 EP 1990-905859 19900323; CA 2013573 C CA 1990-2013573 19900330; JP 3004049 B2

JP 1990-505536 19900323, WO 1990-US1573 19900323
FDT JP 04504204 W Based on WO 9011687; AU 645489 B Previous Publ. AU 9053560, Based on WO 9011687; EP 465560 B1 Based on WO 9011687; DE 69027313 E Based on EP 465560, Based on WO 9011687; ES 2090129 T3 Based on EP 465560; JP 3004049 B2 Previous Publ. JP 04504204, Based on WO 9011687
PRAI US 1989-331979 19890331; US 1992-981935 19921119

L21 ANSWER 7 OF 7 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1990-068945 [10] WPIDS
DNC C1990-030170
TI Transformed ***Salmonella*** bacterial strains - capable of expression of heterologous genes for use in vaccines and for protein prodn..
DC B04 D16
IN SADOFF, J C; YOUNG, J F
PA (SMIK) SMITHKLINE BECKMAN CORP; (USSA) US SEC OF ARMY; (USGO) USOF AMERICA
CYC 18
PI EP 357208 A 19900307 (199010)* EN 14p
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
AU 8938211 A 19900125 (199010)
PT 91238 A 19900208 (199010)
JP 02084172 A 19900326 (199018)
DK 8903559 A 19900122 (199021)
ZA 8905525 A 19910227 (199113)
ADT EP 357208 A EP 1989-307406 19890720; JP 02084172 A JP 1989-185845 19890717; ZA 8905525 A ZA 1989-5525 19890720
PRAI US 1988-222202 19880721
AB EP 357208 A UPAB: 19930928
A ***Salmonella*** bacterial strain transformed with an ***expression*** ***vector*** comprising a heterologous gene operatively linked to an E. coli promoter sequence is claimed. Also claimed is a vaccine capable of inducing cell-mediated immunity against infection in an animal or human by an infective agent comprising an ***attenuated*** ***Salmonella*** bacterial strain transformed with a vector contg. the coding sequence of all, or a portion of, a gene from the infective agent capable of inducing protective immunity, the gene being under control of an E. coli promoter sequence, and the transformant being capable of constitutive expression of the heterologous gene in vivo.
USE - Vaccines can be obtd. for inducing cell-mediated immunity against infection e.g. malaria using a coding sequence of a circumsporozoite (CS) protein of a Plasmodium species or against a virus such as HIV-1, HIV-2 or HIV-3. The transformed strains can also be used to produce e.g tissue plasminogen activator, interferon or hepatitis B surface antigen. The transformants are capable of constitutive expression of the heterologous gene in vivo.
0/2

L31 ANSWER 13 OF 35 MEDLINE
1998114379 Document Number: 98114379. Comparison of the abilities of different ***attenuated*** ***Salmonella*** typhimurium strains to elicit humoral immune responses against a ***heterologous*** antigen. Dunstan S J; Simmons C P; Strugnell R A. (Department of Microbiology and Immunology, University of Melbourne, Parkville, Victoria, Australia.. s.dunstan@pgrad.unimelb.edu.au) . INFECTION AND IMMUNITY, (1998 Feb) 66 (2) 732-40. Journal code: GO7. ISSN: 0019-9567. Pub. country: United States. Language: English.
AB We compared the abilities of different ***Salmonella*** enterica var. Typhimurium (S. typhimurium) strains harboring mutations in the genes aroA, aroAD, purA, ompR, htrA, and cya crp to present the ***heterologous*** antigen, C fragment of tetanus toxin, to the mouse

immune system. Plasmid pTETtac4, encoding C fragment, was transferred into the various S. typhimurium mutants, and the levels of antigen expression were found to be equivalent. After primary oral immunization of BALB/c mice, all ***attenuated*** strains were capable of penetrating the gut epithelium and colonizing the Peyer's patches and spleens of mice. Of all strains compared, the delta purA mutant colonized and persisted in the Peyer's patches at the lowest level, whereas the delta htrA mutant colonized and persisted in the spleen at the lowest level. The level of specific antibody elicited by the different strains against either S. typhimurium lipopolysaccharide or tetanus toxoid was strain dependent and did not directly correlate to the mutants' ability to colonize the spleen. The level of immunoglobulin G1 (IgG1) and IgG2a antibody specific for tetanus toxoid was determined in mice immunized with four S. typhimurium mutants. The level of antigen-specific IgG1 and IgG2a was significantly lower in animals immunized with S. typhimurium delta purA. Antigen-specific T-cell proliferation assays indicated a degree of variability in the capacity of some strains to elicit T cells to the ***heterologous*** antigen. Cytokine profiles (gamma interferon and interleukin-5) revealed that the four S. typhimurium mutants tested induced a Th1-type immune response. Mice were challenged with a lethal dose of tetanus toxin 96 days after oral immunization. With the exception of the S. typhimurium delta purA mutant, all strains elicited a protective immune response. These data indicate that the level of total Ig specific for the carried antigen, C fragment, does not correlate with the relative invasiveness of the ***vector*** , but it is determined by the carrier mutation and the background of the S. typhimurium strain.

L31 ANSWER 14 OF 35 MEDLINE
97321770 Document Number: 97321770. A murine model of intranasal immunization to assess the immunogenicity of ***attenuated*** ***Salmonella*** typhi live ***vector*** ***vaccines*** in stimulating serum antibody responses to expressed ***foreign*** antigens. Galen J E; Gomez-Duarte O G; Losonsky G A; Halpern J L; Lauderbaugh C S; Kaintuck S; Reymann M K; Levine M M. (Department of Medicine, University of Maryland School of Medicine, Baltimore 21201-1509, USA.) VACCINE, (1997 Apr-May) 15 (6-7) 700-8. Journal code: X60. ISSN: 0264-410X. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The lack of a practical small animal model to study the immunogenicity of ***Salmonella*** typhi-based live ***vector*** ***vaccines*** expressing ***foreign*** antigens has seriously impeded the ***vaccine*** development process. For some ***foreign*** antigens, stimulation of serum IgG antibody is the desired, protective immune response. We administered to mice, by orogastric or intranasal (i.n.) routes, ***attenuated*** delta aroC delta aroD S. typhi CVD 908 carrying a plasmid encoding fragment C (fragC) of tetanus toxin fused to the eukaryotic cell receptor binding domain of diphtheria toxin (fragC-bDt), and monitored serum antibody. While orogastric inoculation of three doses was not immunogenic, i.n. immunization elicited high titers of serum IgG tetanus antitoxin, generating peak ELISA geometric mean titers (GMT) of 27024 and 35658 with 10(8) and 10(9) c.f.u. dosages, respectively; 10(9) c.f.u. i.n. of an delta aroA S. typhimurium live ***vector*** stimulated a peak antitoxin GMT of 376 405. Mice immunized with the S. typhi live ***vector*** were 100% protected against challenge with 100 50% lethal doses of tetanus toxin that rapidly killed all control mice. Intranasal immunization with two doses of S. typhi expressing unfused fragment C under control of an anaerobically-activated promoter derived from nirB stimulated significantly higher titers of serum neutralizing antitoxin than fused fragC-bDt controlled by the same promoter (GMT 0.10 AU ml-1 vs 0.01 AU ml-1, P = 0.0095). Two i.n. doses of

S typhi encoding fragC under control of powerful constitutive promoter lpp led to significantly higher peak serum neutralizing antitoxin titers than the otherwise identical construct utilizing the nirB promoter (peak GMT 0.72 AU ml-1 vs 0.10 AU ml-1, P = 0.022). The i.n. route of inoculation of mice may constitute a practical breakthrough that could expedite the development of some S. typhi-based live ***vector*** ***vaccines*** by allowing, for the first time, quantitative measurement of serum antibody responses to candidate constructs following i.n. mucosal immunization.

L31 ANSWER 15 OF 35 MEDLINE

97230322 Document Number: 97230322. Mucosal immunogenicity of a recombinant ***Salmonella*** typhimurium-cloned ***heterologous*** antigen in the absence or presence of coexpressed cholera toxin A2 and B subunits. Harokopakis E; Hajishengallis G; Greenway T E; Russell M W; Michalek S M. (Department of Microbiology, University of Alabama at Birmingham, 35294, USA.) INFECTION AND IMMUNITY, (1997 Apr) 65 (4) 1445-54. Journal code: G07. ISSN: 0019-9567. Pub. country: United States. Language: English.

AB An ***avirulent*** ***Salmonella*** typhimurium ***vaccine*** strain expressing a streptococcal protein adhesin and a similar clone which produces the same streptococcal antigen linked to the cholera toxin (CT) A2 and B subunits (CTA2/B) were compared for the ability to induce antibody responses to the expressed ***heterologous*** antigen after oral or intranasal immunization of mice. Expression of cloned immunogens in these systems is temperature regulated, being optimal at 37 degrees C, and the two clones under comparison were shown to produce similar levels of the streptococcal antigen. Both clones were found to stimulate high levels of serum immunoglobulin G (IgG) and mucosal IgA antibodies to the cloned immunogen. A consistent trend was observed toward higher mucosal IgA but lower serum IgG responses in the case of the S. typhimurium ***vector*** that coexpressed CTA2/B, a potential mucosal adjuvant, regardless of the route of administration. Also noteworthy was the capacity of these antigen delivery systems to induce anamnestic systemic and secretory responses to the cloned immunogen 15 weeks after the primary immunization, despite preexisting immunity to the ***Salmonella*** vectors. These antibody responses were sustained for at least 7 months following the booster immunization, at which time the secretory IgA antibody levels were significantly higher in mice given the ***Salmonella*** clone that coexpressed CTA2/B. Although the serum IgG response against the ***Salmonella*** ***vector*** was characterized by a high IgG2a/IgG1 ratio (indicative of the T helper type 1 [Th1]/Th2 profile), a mixed IgG1 and IgG2a pattern was observed for the carried ***heterologous*** antigen, which displayed a dominant IgG1 response when administered as a purified immunogen. Our findings indicate that the recombinant streptococcal antigen and CTA2/B are strong immunogens when expressed by the antigen delivery system used in this study and suggest that CTA2/B may have an additional immunoenhancing activity in the mucosal compartment besides its ability to target antigen uptake into the mucosal inductive sites. CTA2/B may thus be useful as an S. typhimurium-cloned adjuvant for coexpressed protein antigens.

L31 ANSWER 16 OF 35 MEDLINE

97218595 Document Number: 97218595. Oral delivery of ***foreign*** antigens by ***attenuated*** ***Salmonella*** : consequences of prior exposure to the ***vector*** strain. Attridge S R; Davies R; LaBrooy J T. (Department of Microbiology and Immunology, University of Adelaide, Australia.) VACCINE, (1997 Feb) 15 (2) 155-62. Journal code: X60. ISSN: 0264-410X. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Several strains of ***Salmonella*** have been used as vectors for the delivery of Escherichia coli fimbrial proteins to the gut-associated lymphoid tissue (GALT) of the mouse. Plasmids carrying a complementing thyA+ gene, together with genes specifying synthesis of K88 or K99, were introduced into non-reverting thyA ***Salmonella*** mutants. The resulting constructs expressed the ***foreign*** pilin protein on their surfaces and, provided the ***vector*** was able to colonize the GALT, elicited strong serum responses to K88 or K99. These responses were dramatically impaired however, in recipients with pre-existing immunity to the ***vector*** strain. Mice initially infected with ***Salmonella*** stanley ca 4, 10 or 20 weeks prior to oral administration of S. stanley-K88 showed greatly reduced serum responses to K88 as determined by ELISA. The hypo-responsiveness seen in ***vector*** -primed mice could be largely overcome by changing the serotype of the strain subsequently used to deliver the ***foreign*** protein.

L31 ANSWER 17 OF 35 MEDLINE
97170762 Document Number: 97170762. Protective immunity against herpes simplex virus (HSV) type 1 following oral administration of recombinant ***Salmonella*** typhimurium ***vaccine*** strains expressing HSV antigens. Karem K L; Bowen J; Kuklin N; Rouse B T. (Department of Microbiology and Immunology, College of Veterinary Medicine, University of Tennessee at Knoxville, 37996, USA.) JOURNAL OF GENERAL VIROLOGY, (1997 Feb) 78 (Pt 2) 427-34. Journal code: I9B. ISSN: 0022-1317. Pub. country: ENGLAND: United Kingdom. Language: English.

AB ***Salmonella*** typhimurium strains expressing ***foreign*** antigens of various pathogens are capable of eliciting antigen-specific humoral and cellular immune responses. ***Attenuated*** S. typhimurium strain chi4550 (delta(cya) delta(crp) delta(asd)) was used as an expression ***vector*** for herpes simplex virus (HSV) antigens. Genes encoding glycoprotein D (gD) and the immediate-early protein ICP27 of HSV-1 were cloned and expressed in plasmid pYA292 (asd+) and subsequently placed into chi4550. Following two oral immunizations, the protective efficacy of recombinant strains against zosteriform challenge with HSV-1 was measured in 3-4-week-old BALB/c mice. Levels of protection observed were 77% with the ICP27 construct but only 31% with the gD construct. Zosteriform protection correlates with a CD4+-mediated delayed-type hypersensitivity (DTH) reaction against HSV. Accordingly, significant DTH was observed only in mice immunized orally with the S. typhimurium ICP27 construct. ELISA analysis of antigen-specific humoral responses failed to detect serum antibody responses following oral administration although recombinant S. typhimurium were isolated from spleens of orally dosed mice up to day 30. Intravenous (i.v.) immunization with the gD-expressing construct did, however, induce detectable serum antibody responses. Some humoral IgA responses against gD in faecal samples were detected as early as 3 weeks post-oral immunization while those induced by the i.v. route were slightly lower. These data suggest that recombinant S. typhimurium HSV antigens are capable of inducing immunity against HSV, some aspects of which are protective against HSV challenge.

L31 ANSWER 18 OF 35 MEDLINE
97075209 Document Number: 97075209. Induction of an antibody response in mice against human papillomavirus (HPV) type 16 after immunization with HPV recombinant ***Salmonella*** strains. Krul M R; Tijhaar E J; Kleijne J A; Van Loon A M; Nievers M G; Schipper H; Geerse L; Van der Kolk M; Steerenberg P A; Mooi F R; Den Otter W. (European Cancer Centre, Amsterdam, The Netherlands.. ecc@euronet.nl) . CANCER IMMUNOLOGY, IMMUNOTHERAPY, (1996 Sep) 43 (1) 44-8. Journal code: CN3. ISSN: 0340-7004. Pub. country: GERMANY: Germany, Federal Republic of. Language:

English.

AB Human papillomaviruses (HPV) are present in approximately 95% of all cervical carcinomas and the HPV E6 and E7 genes are continuously expressed in these lesions. There is also circumstantial evidence that often natural immunity against HPV is generated and that this is of influence on HPV-induced lesions. Stimulation of the immune system by proper presentation of relevant HPV antigens might, therefore, lead to a prophylactic or therapeutic immunological intervention for HPV-induced lesions. For this purpose we have expressed the E6 and E7 protein of HPV 16 in an ***attenuated*** strain of ***Salmonella*** typhimurium (SL3261, aroA mutation), which has been used extensively as a live ***vector*** . Live recombinant ***Salmonella*** ***vaccines*** have the ability to elicit humoral, secretory and cell-mediated immune responses, including cytotoxic T cells, against the ***heterologous*** antigens they express. This report describes the construction of recombinant ***Salmonella*** strains expressing the HPV 16 E6 and E7 proteins, and the induction of an HPV-16-specific immune response in mice after immunization with these live vectors.

L31 ANSWER 19 OF 35 MEDLINE

96363710 Document Number: 96363710. Construction and immunogenicity of ***Salmonella*** typhimurium ***vaccine*** vectors that express HIV-1 gp120. Fouts T R; Tuskan R G; Chada S; Hone D M; Lewis G K. (Department of Geographic Medicine, School of Medicine, University of Maryland at Baltimore 21201, USA.) VACCINE, (1995 Dec) 13 (17) 1697-705. Journal code: X60. ISSN: 0264-410X. Pub. country: ENGLAND: United Kingdom. Language: English.

NOT IN LIBRARY

AB Since the human immunodeficiency virus (HIV-1) is transmitted either parenterally or sexually, both mucosal and systemic immune responses may be required to provide protective immunity. ***Attenuated*** ***Salmonella*** vectors expressing ***heterologous*** antigen can stimulate responses in both compartments. To evaluate the utility of ***Salmonella*** vectors as an HIV-1 ***vector*** ***vaccine*** a gene expression cassette encoding recombinant HIV-1 gp120 (rgp120) was integrated into the hisOGD locus of ***Salmonella*** typhimurium aroA strain, SL3261 (SL3261::120). To test if increased antigen expression potentiates immunogenicity, strains were constructed that express rgp120 from a multicopy asd-stabilized plasmid (SL7207 pYA:120). Immunoblot analysis demonstrated that SL7207 pYA:120 expressed approximately 50-fold more rgp120 than SL3261::120. Oral immunization of BALB/c mice with these strains did not stimulate an env-specific CTL response or a significant rise in antigp120 antibody titer as compared to controls. However, splenic T cells from SL7207 pYA::120 immunized mice proliferated upon restimulation with gp120 in vitro while splenocytes from SL3261::120 immunized mice did not, gp120 restimulated splenic T cells from SL7207 pYA:120 immune mice also produced IFN-gamma but no IL-5. Two conclusions can be drawn from these results. First, high level expression of rgp120 in ***Salmonella*** vectors is necessary to stimulate a gp120-specific immune response in mice. Second, ***Salmonella*** ::rgp120 stimulates a gp120-specific Th1 response in mice. This is the first report to describe the construction of a ***Salmonella*** ::rgp120 ***vector*** ***vaccine*** that is immunogenic in mice.

L31 ANSWER 20 OF 35 MEDLINE

96351471 Document Number: 96351471. ***Attenuated*** ***Salmonella*** as live oral ***vaccines*** against typhoid fever and as live vectors. Levine M M; Galen J; Barry E; Noriega F; Chatfield S; Sztein M; Dougan G; Tacket C. (Center for Vaccine Development, University of Maryland School of Medicine, Baltimore 21201, USA.) JOURNAL OF BIOTECHNOLOGY, (1996 Jan

26) 44 (1-3) 193-6. Ref: 19. Journal code: AL6. ISSN: 0168-1656. Pub. country: Netherlands. Language: English.

AB ***Attenuated*** ***Salmonella*** typhi ***vaccine*** strain CVD 908, which harbors deletion mutations in aroC and aroD, has been shown to be well-tolerated and highly immunogenic, eliciting impressive serum antibody, mucosal IgA and cell-mediated immune responses. A further derivative prepared by introducing a deletion in htrA (which encodes a heat-shock protein that also has activity as a serine protease in CVD 908 (Chatfield et al., unpublished data) resulted in CVD 908-htrA. In phase 1 clinical trials, CVD 908-htrA appears very attractive as a live oral ***vaccine*** candidate. Both CVD 908 and CVD 908-htrA are useful as live ***vector*** ***vaccines*** to deliver ***foreign*** antigens to the immune system. Conditions that enhance the expression and immunogenicity of ***foreign*** antigens carried by CVD 908 and CVD 908-htrA are being investigated.

L37 ANSWER 13 OF 14 USPATFULL
94:15647 Process for secretory production of a calcium-binding protein.
Zenno, Shuhei, Yokohama, Japan
Inouye, Satoshi, San Diego, CA, United States
Chisso Corporation, Osaka, Japan (non-U.S. corporation)
US 5288623 19940222
APPLICATION: US 1992-912582 19920713 (7)
PRIORITY: JP 1989-279528 19891026
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A process for secretory production of a calcium-binding protein very useful for producing heterogenic proteins in Escherichia ***coli*** according to gene recombinant technique is provided, which process comprises using Escherichia ***coli*** and using a secretory expression system with the promoter of ***lipoprotein*** and the gene of signal peptide of ***outer*** ***membrane*** ***protein*** A, according to recombinant DNA technique.

L37 ANSWER 12 OF 14 USPATFULL
94:82162 Expression of proteins on bacterial surface.
Georgiou, George, 11501 Juniper Ridge Dr., Austin, TX, United States 78759
Francisco, Joseph A., Austin, TX, United States
Earhart, Charles F., Austin, TX, United States
Georgiou, George, Austin, TX, United States (U.S. individual)
US 5348867 19940920
APPLICATION: US 1991-794731 19911115 (7)
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to a method for producing stable, surface-expressed polypeptides from recombinant gram-negative bacterial cell hosts. A tripartite chimetic gene and its related recombinant vector include separate DNA sequences for directing or targeting and translocating a desired gene product from a cell periplasm to the external cell surface. A wide range of polypeptides may be efficiently surface expressed, including .beta.-lactamase and alkaline phosphatase. Full enzyme activity is maintained and the proteins remain anchored to the bacterial outer membrane surface.

CLM What is claimed:
1. A recombinant DNA for expressing a polypeptide stably anchored on the external surface of the outer membrane of E. ***coli*** or Salmonella comprising: (A) A Salmonella or E. ***coli*** ***lipoprotein*** 5' gene segment which encodes at least the ***signal*** peptide and at least the first three amino acids of the

mature protein; (B) A DNA segment encoding a transmembrane ***outer*** ***membrane*** ***protein*** selected from the group consisting of ***OmpA*** , OmpC, OmpF and OmpT of E. ***coli*** or Salmonella; and (C) A DNA segment encoding a desired soluble heterologous or homologous polypeptide not normally found in the outer membrane of gram negative bacteria wherein DNA (A) is linked 5' to DNA (B) and DNA (B) is linked 5' to DNA (C), all operatively linked with a promoter sequence to express and anchor the desired polypeptide on the external bacterial surface.

2. A recombinant DNA vector comprising: An E. ***coli*** or Salmonella ***lipoprotein*** 5' gene segment which encodes the ***signal*** peptide and at least the first three amino acids of the mature protein; A DNA segment encoding a transmembrane ***outer*** ***membrane*** ***protein*** selected from the group consisting of ***OmpA*** , OmpT, OmpF and OmpC of E. ***coli*** or Salmonella; and A polylinker DNA segment into which a DNA encoding soluble heterologous or homologous polypeptide not normally found in the outer membrane of gram-negative bacteria may be inserted, all being operatively linked 5' to 3' with a promoter sequence to express and stably anchor the polypeptide to the external bacterial surface.

3. The recombinant DNA of claim 1 or the recombinant vector of claim 2 wherein the ***lipoprotein*** gene segment comprises the 5' segment of a gene selected from a group consisting of osmB, traT, NlpB, and Psuedomonas ***lipoprotein*** 1.

4. The recombinant DNA of claim 1 or the recombinant vector of claim 2 wherein the DNA encoding the ***lipoprotein*** gene segment encodes the N-terminal amino acid residues of FIG. 7 (SEQ ID NO. 1) at base pair positions 1-87.

5. The recombinant DNA of claim 1 or the recombinant vector of claim 2 wherein the transmembrane protein domain comprises an amino acid sequence of FIG. 7 (SEQ ID NO. 1) at base pairs 94-435.

6. The recombinant DNA of claim 1 or the recombinant vector of claim 2 wherein the promoter is an inducible promoter.

7. The recombinant DNA or the recombinant vector of claim 6 wherein the inducible promoter is Lpp or lac promoter.

8. An Escherichia ***coli*** transformed with a vector containing the DNA of claim 1.

9. A Salmonella transformed with a vector containing the DNA of claim 1.

10. A method of preparing a functional polypeptide stably anchored on the external surface of the outer membrane of a bacterial cell comprising growing the bacterial host cell of claim 8 or claim 9 under conditions permitting DNA expression and protein production followed by recovering the stably anchored polypeptide so produced.

11. The method of claim 10 wherein the growing is conducted between about 22.degree. C. and 40.degree. C.

12. The method of claim 10 wherein the growing is conducted at about 24.degree. C.

13. The recombinant DNA of claim 1 wherein the soluble homologous polypeptide is .beta.-lactamase or alkaline phosphatase.

14. The recombinant DNA of claim 1 wherein the heterologous polypeptide is a single chain antibody or antibody fragment.

15. A kit for use in preparing transformed E. ***coli*** or Salmonella comprising an expression vector that includes the recombinant DNA of claim 1.

16. The kit of claim 15 wherein the expression vector has the sequence shown in FIG. 7 (SEQ ID NO: 1).

17. The kit of claim 15 wherein the expression vector is provided in lyophilized form or in a suitable buffer.

18. The recombinant DNA of claim 1 wherein the heterologous polypeptide is cellulose binding domain of cellulase.

19. The recombinant DNA of claim 1 wherein the encoded transmembrane protein is a transmembrane sequence of ***OmpA*** .

L37 ANSWER 13 OF 14 USPATFULL
94:15647 Process for secretory production of a calcium-binding protein.
Zenno, Shuhei, Yokohama, Japan
Inouye, Satoshi, San Diego, CA, United States
Chisso Corporation, Osaka, Japan (non-U.S. corporation)
US 5288623 19940222
APPLICATION: US 1992-912582 19920713 (7)
PRIORITY: JP 1989-279528 19891026
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A process for secretory production of a calcium-binding protein very useful for producing heterogenic proteins in Escherichia ***coli*** according to gene recombinant technique is provided, which process comprises using Escherichia ***coli*** and using a secretory expression system with the promoter of ***lipoprotein*** and the gene of signal peptide of ***outer*** ***membrane*** ***protein*** A, according to recombinant DNA technique.

CLM What is claimed is:
1. A process for producing a ***fusion*** ***protein*** comprising a calcium-binding protein and biogenic substance of E. ***coli*** which facilitates the extracellular secretory production of the ***fusion*** ***protein*** , which process comprises: preparing a recombinant plasmid as a cloning vehicle for expression of the ***fusion*** ***protein*** in E. ***coli*** , said plasmid comprising a first DNA sequence consisting of a ***lipoprotein*** promoter region being linked in reading phase with a second DNA sequence located downstream of said first DNA sequence, said second DNA sequence coding for a ***signal*** peptide of ***outer*** ***membrane*** ***protein*** A and being linked in reading phase with a third DNA sequence located downstream of said second DNA sequence, said third DNA sequence coding for the ***fusion*** ***protein*** , inserting said plasmid into E. ***coli*** to obtain a transformed E. coliand cultivating the transformed E. ***coli*** in a suitable medium to produce said ***fusion*** ***protein*** , wherein said calcium-binding protein is selected from the group consisting of calmodulin, troponin c, myosin

light chain, parvalubumin, vitamin D-dependent calcium-binding proteins, S-100, S-100.beta., calpactin, carpaine/CANP, and oncomodulin.

2. A process for producing a ***fusion*** ***protein*** comprising apoaequorin and a biogenic substance in E. ***coli*** which facilitates the extracellular secretory production of the ***fusion*** ***protein*** , which process comprises: preparing a recombinant plasmid as a cloning vehicle for expression of the ***fusion*** ***protein*** in E. ***coli*** , said plasmid comprising a first DNA sequence consisting of a ***lipoprotein*** promoter region being linked in reading phase with a second DNA sequence located downstream of said first DNA sequence, said second DNA sequence coding for a ***signal*** peptide of ***outer*** ***membrane*** ***protein*** A and being linked in reading phase with a third DNA sequence located downstream of said second DNA sequence, said third DNA sequence coding for the ***fusion*** ***protein*** , inserting said plasmid into E. ***coli*** to obtain a transformed E. ***coli*** , and cultivating the transformed E. ***coli*** in a suitable medium to produce said ***fusion*** ***protein*** .

L44 ANSWER 9 OF 26 MEDLINE
96084971 Document Number: 96084971. A novel Escherichia coli lipoprotein expression vector. Jones T S; Tryon V V. (Department of Microbiology, University of Texas Health Science Center at San Antonio 78284-7758, USA..) GENE, (1995 Nov 7) 165 (1) 145-6. Journal code: FOP. ISSN: 0378-1119. Pub. country: Netherlands. Language: English.

AB A novel Escherichia coli (Ec) lipoprotein expression plasmid, pSJLP, was constructed. The plasmid contains a truncated alkaline phosphatase gene (phoA) located downstream from the Lac repressor gene lacIq and the IPTG inducible Ptac promoter. The phoA gene was truncated by deleting the native phoA signal sequence and fusing the truncated phoA gene to the ***lipoprotein*** ***signal*** ***sequence*** of the major Ec lipoprotein LPP. The recombinant LPP::PhoA fusion protein is produced and processed as a lipoprotein and can therefore be used as substrate for a novel signal peptidase II assay.

L44 ANSWER 20 OF 26 MEDLINE
92153029 Document Number: 92153029. A colicin M derivative containing the ***lipoprotein*** ***signal*** ***sequence*** is secreted and renders the colicin M target accessible from inside the cells. Olschlager T. (Mikrobiologie II, Universitat Tubingen, Federal Republic of Germany..) ARCHIVES OF MICROBIOLOGY, (1991) 156 (6) 449-54. Journal code: 7YN. ISSN: 0302-8933. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Colicin M is only released in very low amounts by cells harbouring this plasmid encoded colicin, due to the lack of a release (lysis) protein. A fusion gene (lpp'cma) was constructed which determined two proteins: Lpp'-Cma composed of the signal sequence of the murein lipoprotein (Lpp) and colicin M (Cma), and unaltered colicin M. Cells expressing the fusion gene released 50% of the total colicin M into the culture medium, compared to 1% found in the medium of cells synthesizing only colicin M. The release resulted from partial cell lysis caused by colicin M since a colicin M tolerant strain remained unaffected. Lpp'-Cma thus mimics phenotypically the action of colicin release proteins but displays a different lysis mechanism. In strains defective in components of the colicin M uptake system, Lpp'-Cma caused lysis as effectively as in uptake proficient strains. Apparently, Lpp'-Cma renders the colicin M target site accessible from inside the cell which stands in contrast to the action of

colicin M which is only bactericidal when provided from outside.

L44 ANSWER 26 OF 26 MEDLINE
83223595 Document Number: 83223595. Requirement for signal peptide cleavage of Escherichia coli prolipoprotein. Inouye S; Hsu C P; Itakura K; Inouye M. SCIENCE, (1983 Jul 1) 221 (4605) 59-61. Journal code: UJ7. ISSN: 0036-8075. Pub. country: United States. Language: English.
AB Oligonucleotide-directed site-specific mutagenesis was applied to alter the cleavage site in the signal peptide of the major outer membrane lipoprotein of Escherichia coli. Replacing the glycine residue at the cleavage site with an alanine residue did not affect the processing of the signal peptide. However, when the same cleavage site was constructed by the deletion of the glycine residue, the signal peptide was no longer cleaved. These results indicate that stringent structural integrity at the cleavage site in the ***lipoprotein*** ***signal*** ***sequence*** is required for correct processing of prolipoprotein.